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AN EXPERIMENTAL STUDY[1] OF URETERO-INTESTINAL IMPLANTATION

I. THE CAUSE OF PERITONITIS

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NO method of uretero-intestinal implantation in general use has proved its outstanding superiority. Probably the manner of execution (technique) is as much at fault as the method which is used. Poor workmanship in the performance of the operation can be responsible for as many failures as the flaws in the method itself. The brilliant successes which have been obtained occasionally by almost any of the many different methods which have been used, lead to the conviction that uretero-intestinal implantation is feasible and that a method which is superior is possible; in other words, that a plan of operation will become sufficiently standardized, even when put to general use, to minimize failures. The method must be planned not only to prevent the complications which cause failure but also to permit good performance by different surgeons. This demands simplicity of technique.

The immediate risks of ureteral implantation, aside from shock, pneumonia, etc., are:

1. Infection: (a) peritonitis, both local and general; (b) infection of the abdominal wound; (c) infection about the ureter where it enters the bowel, which may lead to peritonitis or ureteritis; (d) ureteritis and pyelonephritis (both ascending and hematogenous).

2. Ureteral obstruction which has a variety of causes, such as: (a) surgical edema; (b) constriction and kinks caused by the method and manner of anastomosis; (c) bands and adhesions; (d) inflammation, periureteral, interureteral, and intra-ureteral; (e) anemic necrosis; (f) neurogenic stasis, ureteral atony, and dilatation.

Many of these complications are more imminent with some methods than others. For this reason perhaps the incidence of peritonitis varies in the different statistical reports. For example, Ssolowoff gave peritonitis as the cause of death in 10 of the 14 deaths in his series of 30 cases, and Coffey, in 4 of the 9 deaths in 35 cases (Table I). Cabot reported 14 consecutive uretero-intestinal implantations for exstrophy of the bladder without an operative death. However, 21 of Ssolowoff's patients had vesical carcinoma and only 1 had exstrophy. Seventeen of Coffey's patients had cancer and 10 had exstrophy. Furthermore, in Mayo's experience, transplantation of each ureter separately, for exstrophy in children, is safer than simultaneous bilateral implantation. It is necessary, therefore, to analyze different reports not only with respect to the factors of method and technique as affecting the results, but also with regard to the ages

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and the conditions of the patients. Two of the 4 deaths from peritonitis reported by Coffey were in children with exstrophy. One of my patients with carcinoma of the bladder died of peritonitis following cystectomy 6 weeks after the ureteral implantation. This death bore no relation to the implantation. It may be stated, however, that, irrespective of the method used, of the condition for which it is used, or of the age of the patient, peritonitis appears frequently in the statistical reports on uretero-intestinal implantation as being the cause of failure.

It is reasonable to assume that the peritonitis in these cases was caused by leakage at the site of the implantation after the operation had been completed and not by contamination at the time of operation. It is very important that these two sources of infection be distinguished. When this is done, opening the bowel does not appear so prohibitive, and the elaborate methods recently designed by Higgins (1932) and by Poth (1935) to prevent contamination at the time of transplantation are not so essential.

A great deal of work on intestinal resection and anastomosis has shown that the peritoneal cavity can care for considerable contemporary contamination. However, the least bit of leakage because of imperfect suturing, or sutures tearing out after closure, invariably is fatal. Almost 50 years ago (1887), Halsted completed an experimental study of intestinal suture. This contribution developed certain facts which remain today as the fundamentals in intestinal surgery and can be read with profit by every urologist doing uretero-intestinal implantations. He wrote: "We are brought, therefore, to the conclusion that the chief danger of infection of the peritoneum is from the passage of the intestinal contents (bacteria) into the peritoneal cavity *subsequent* to the operation. The conditions which may lead to this unfortunate occurrence are (1) failure to close completely and firmly the wound of the intestine; (2) penetration of the intestinal lumen by one or more sutures; (3) giving way of the sutures; (4) ulceration or sloughing of the intestine at the site of suture." These four conditions which cause peritonitis subsequent to intestinal resection occur likewise following implantation of the ureter. Halsted's next statement: "In order to bring about complete and firm closure of the abnormal opening into the intestine, it has been customary to make several series of sutures of the intestine one over the other in the form of the so called *Étagennaht*. In this way a considerable extent of the intestinal wall is folded in, the circulation of which is greatly impeded. There are especial dangers which attend the folding in of an unnecessarily large amount of intestinal wall, for, on the one hand, this increases the extent of tissue which undergoes sloughing and thus increases the danger of infection, and, on the other hand, the flange formed by the folds projecting into the intestinal lumen is an obstacle to the passage downward of the feces, which, accumulating at and above the site of suture, increase the tension upon the sutures and endanger their separation." Applying these principles to the problem of ureteral implantation, it is evident that, in addition to the risks of sloughing and giving way of the sutures, a method of closure in layers by rows of sutures increases the likelihood of ureteral constriction. The need of a simple method of closure is obvious. Furthermore, the added suturing of the intestinal wall required by closure in layers increases the chance of one or more of these sutures accidentally penetrating the intestinal lumen. Finally, to quote Halsted further, "Any one, by a simple experiment, can convince himself how frail is the hold of sutures which include only serosa and muscularis. I am inclined to regard perforation of the gut wall, on the one hand, and tearing out of stitches, on the other, as the leading factors in the production of the peritonitis which has brought about the fatal issue in many cases of intestinal suture."

The causative factors producing peritonitis, such as method on the one hand and technique on the other, may be studied experimentally, and the following pages present such a study.

EXPERIMENTAL STUDY OF THE CAUSE OF PERITONITIS

Ureteral implantation, simultaneously bilateral except in two instances (serial Nos. 28 and 50, Table II), was performed on 53 dogs

TABLE I

Condition	Surgeon	Number of patients	After implantation		After cystectomy		Total		
			Living	Dead	Living	Dead	Living	Dead	Died of peritonitis
Urethral occlusion	Ssolowoff	3	1	2					
Ureterovaginal fistula	Ssolowoff	1	1						
Hunner ulcer	Personal	1		1					
Vesicovaginal fistula	Ssolowoff	3	1	2					
	Coffey	4	3	1					
	Personal	4	2	2					
Tuberculous ulcers of the bladder	Ssolowoff	1	1						
	Coffey	4	3	1					
	Personal	7	7						
Exstrophy of the bladder	Ssolowoff	1		1					
	Coffey	10		3	6	1			
	Personal	11		1	7	3			
Carcinoma of the bladder	Ssolowoff	21	4	7	8	2			
	Coffey	17		8	6	3			
	Personal	17	3	3	5	6			
Summary	Ssolowoff	30	8	12	8	2	16	14	10
	Coffey	35	6	13	12	4	18	17	4
	Personal	40	12	7	12	9	24	16	2
Total		105	26	32	32	15	58	47	16

by 10 different methods (Table II). The bowel was opened at the time of the operation in all but the 5 dogs on which Higgins' method was used. In 40 dogs (serial Nos. 9 to 48 inclusive, Table II) variation of technique was slight and is indicated sufficiently by the accompanying drawings. Thirteen of the 53 dogs died of peritonitis. The experiments were not planned solely for the study of peritonitis. The poor results obtained were fully anticipated in most cases. The significance of suturing and overlapping of the bowel to necrosis and leakage, fully demonstrated by Halsted and others, needs no confirmatory study. The results, however, indicate, as anyone might predict, that the risk of peritonitis is much greater by some methods than by others.

A. Experimental evidence of contamination at the time of operation as a cause of peritonitis. Experimental and clinical experience in intestinal suturing minimizes the risk of peritonitis from contamination with intestinal contents at the time of operation. This conclusion was tested personally on dogs a number of times: The bowel was incised and opened as for ureteral implantation. Instead, a probe was inserted and well soiled, then withdrawn and the dirty end smeared about over the bowel and neighboring loops. The incision in the bowel then was closed. None of these dogs showed any evidence of local or general peritonitis.

In the course of opening the bowel 96 times in the 48 dogs for the implantation of ureters, gross contamination occurred at this time in 6; by the leaking out of the contents of the bowel in 2, and by the ureter's slipping out, or having to be withdrawn after insertion and reinserted, in 4. Considerable soiling of the operative field was obvious in these 6 cases, and it probably occurred to a lesser degree in others. In none was this type of contamination responsible for peritonitis. Nevertheless this source of contamination is a potential risk and the plan of any operation should be to reduce it to a minimum by proper preoperative preparation of the bowel and by the

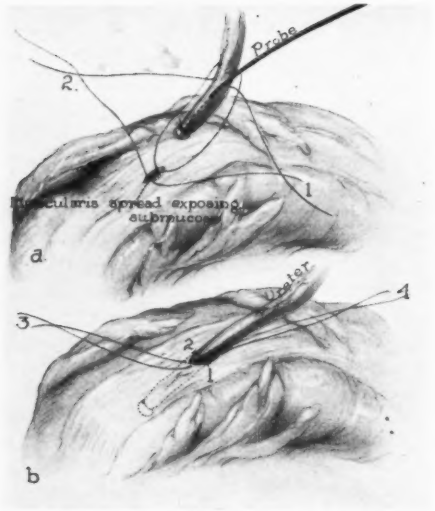

Fig. 1.

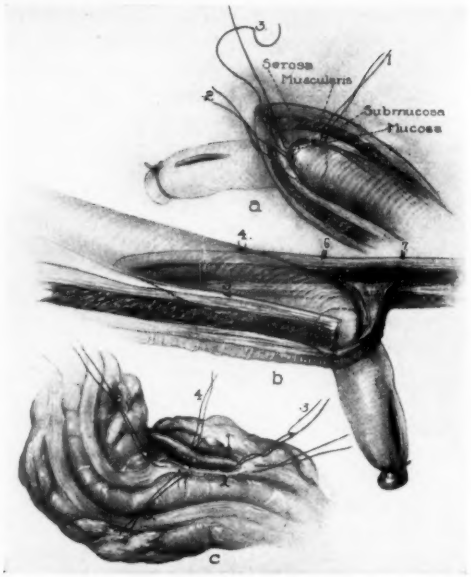

Fig. 2.

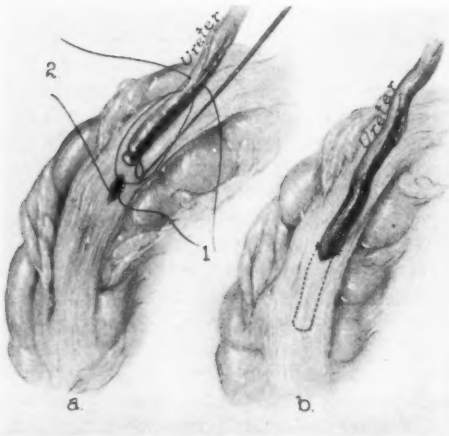

Fig. 3.

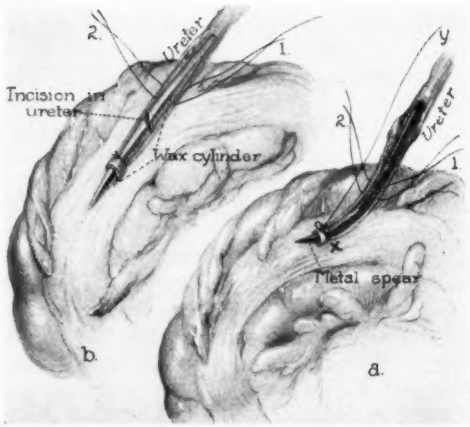

Fig. 4.

Fig. 1. Direct insertion of the ureter which is anchored with two sutures, *1* and *2*. The short incision is closed with one suture on each end, *3* and *4*. a, The anchoring sutures placed in the submucosa of the intestine and the adventitia of the ureter. b, The end of the ureter has been pushed through a small stab incision of the submucous and mucous layers. Sutures *1* and *2* have been tied. Sutures *3* and *4* close the muscularis about the ureter.

Fig. 2. Diagrammatic representation of the manner in which the ureter is anchored in the wall of the intestine by the simple seven suture method. a, The sutures *1*, *2*, and *3* anchor the ureter snugly in the small opening through the submucosa and mucosa made by the cautery. Note that this slit should not be too large but of a size, as indicated by the dotted circle, equal to the diameter of the ureter. b, The unconstricted anastomosis. c, Sutures *4* and *5* anchor the ureter in the trough of the incision. Sutures *6* and *7* (shown in b) bring together the serous and muscular layers over the point of penetration without constricting the ureter.[1]

Fig. 3. Same as Figure 2 except that the end of the ureter is not slit. The end ligature is left with a loop which is caught by a groove on the end of a probe. After insertion

[1] Application of this method in 12 cases published in detail in Surgery, Gynecology and Obstetrics.

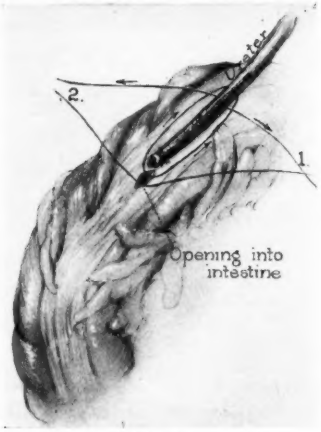

Fig. 5.

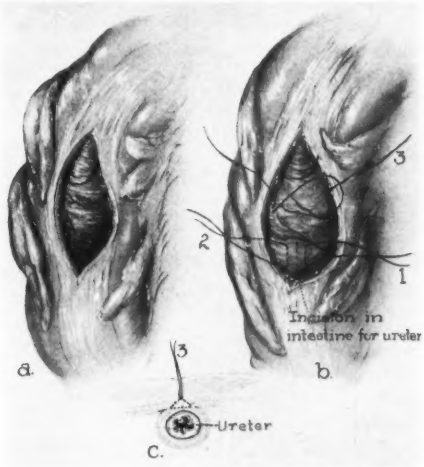

Fig. 6.

Fig. 7.

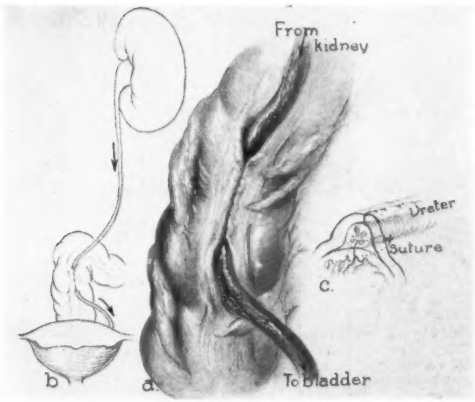

Fig. 8.

of the ligature the loop can be pushed off by the probe, leaving the ureter open at the end.

Fig. 4. Cylinder method of insertion of the ureter without the use of a probe. a, A metal spear is tied in with a bow knot at *x* so that, after insertion, the knot can be untied by pulling the long arm, *y*, and the spear pushed out of the ureter into the bowel. b, A wax cylinder impregnated with merthiolate.

Fig. 5. The use of a segment of a catheter as a cylinder.

Fig. 6. Implantation with a submucous fold. a, Large surface of submucosa exposed. b, Sutures *1* and *2* placed in the submucosa at the lower end and through the adventitia of the ureter (not shown), as in Figure 2. Suture *3* is a mattress so placed that when tied it brings the submucous layer around the ureter completely as shown in c. c, The submucous fold about the ureter.

Fig. 7. A flap of muscularis is made to cover the ureter after insertion.

Fig. 8. Illustrates the method of Coffey-Higgins. a, The undivided and intact ureter (as shown in b) has been imbedded to the submucous layer. c, The hidden suture which cuts through later to form the orifice into the bowel.

use of the best asepsis which is possible with the method used.

B. Experimental evidence of leakage after operation as a cause of peritonitis. Leakage of the contents of the bowel into the peritoneal cavity was demonstrated by distending the bowel at the time of the postmortem examination in 9 of the 13 dogs which died of peritoni-

TABLE II

Method	Serial No.	Group No.	Protocol No.	Date of operation	Date of death	Duration	Cause of death	Remarks
Direct 4 suture method (Fig. 1)	1	1*	232	11-26-34	12- 2-34	6 days	Infection of abdominal wound. Peritonitis	No gross leakage, abscess at site of right implant
	2	2*	238	12- 3-34	12-16-34	13 days	Infection of abdominal wound. Peritonitis	Leakage
	3	3*	237	12- 3-34	12- 6-34	3 days	Infection of abdominal wound. Peritonitis	Leakage
	4	4*	235	12- 4-34	12- 8-34	4 days	Infection of abdominal wound. Peritonitis	Leakage
Partial submucosal method with 6 sutures and ureteral end crushed	5	1*	317	3-20-35	3-26-35	6 days	Infection of wound. Peritonitis	Leakage (right) from necrosis of bowel at site of implantation
	6	2	322	3-20-35	3-29-35	9 days	Infection of abdominal wound. Acute pyelonephritis	
	7	3	308	3-29-35	4- 1-35	3 days	Ureteral reflux; feces in pelvis. Acute pyelonephritis	Ureteral end crushed in angiotribe at time of implantation
	8	4	319	3-29-35	8- 5-35	4 mos.	In poor condition. Killed	Bilateral pyonephrosis
Submucosal 7 suture method. A. Probe and scissors. (Fig. 2)	9	1	332	2- 8-34	9-25-34	7 mos.	Killed	Hydronephrosis on left
	10	2*	300	2-14-34	2-21-34	7 days	Peritonitis	Right ureter pulled loose
	11	3	48	3- 1-34	9-11-34	6 mos.	Killed	Slight bilateral hydronephrosis. Ureteral kink on right
	12	4	77	3-15-34	9-11-34	6 mos.	Killed	Good result
	13	5	81	3-29-34	4- 3-34	4 days	Evisceration	Infection at site of transplant. No leakage
	14	6	80	4- 5-34	4-15-34	10 days	Uremia	Ureteral kink on right; stenosis on left
B. Grooved probe. (Fig. 3)	15	7	103	10-26-34	1- 4-35	2 mos.	Convulsions, cause unknown	Blood urea, 84 on day of death. Moderate hydro-ureter
	16	8	402	10-26-34	10-31-34	4 days	Evisceration	No leakage. Good transplants
	17	9*	151	11- 1-34	11- 3-34	3 days	Retroperitoneal abscess. Peritonitis	Leakage at site of left implant
	18	10	153	11- 1-34	12- 3-34	1 mo.	Infection of abdominal wound. Bilateral pyonephrosis	Ureteral reflux. No leakage
C. Metal spear open. (Fig. 4, a)	19	11	155	11- 7-34	11-16-34	9 days	Left pyonephrosis	Left reflux. Right side is good
D. Wax cylinders (Fig. 4, b)	20	12*	402	4-19-34	(1) Right 9-11-34 (2) Left 10-26-34	5 mos.	Killed 10-31-34, eviscerated	Right hydronephrosis
	21	13	154	11-15-34	12-16-34	1 mo.	Infection of wound. Pyelonephritis	Reflux at left. No leakage
	22	14	156	11-15-34	1-18-35	2 mos.	Killed	Good result
	23	15	233	11-26-34	11-29-34	3 days	Pneumonia	Wound, peritoneum, and transplants in good condition
	24	16	240	12-10-34	4- 2-35	4 mos.	Condition good. Killed	Slight dilatation on both sides
E. End catheter (Fig. 5)	25	17	264	1-24-35	1-27-35	3 days	Acute ascending pyelonephritis (left). Infection of wound	Right kidney appears normal
	26	18	245	1-24-35	1-28-35	4 days	Acute ascending pyelonephritis, bilateral	No peritonitis
F. Probe and cautery	27	19	102	5-24-34	9-11-34	3½ mos.	Killed	Good transplants
	28	20	107	8- 7-34	8-29-34	22 days	Abscess of lung	Slight hydronephrosis. Good transplants
	29	21*	152	8-22-34			Peritonitis	Left ureter had slipped out
	30	22	82	8- 3-34	9-18-34	1½ mos.	Killed	Good transplants
	31	23	101	8- 7-34	8-29-34	22 days	Infection of wound. Pneumonia	Left pyelonephritis. Right side good
	32	24	143	8-14-34	8-27-34	13 days	Uremia	Ureteral obstruction from ureteritis adhesiva

*Died of peritonitis.

TABLE II.—Continued

Method	Serial No.	Group No.	Protocol No.	Date of operation	Date of death	Duration	Cause of death	Remarks
F. Probe and cautery	33	25	144	8-17-34	9-18-34	1 mo.	Killed	Good transplant
	34	26	236	1- 4-35	2- 4-35	1 mo.	Killed	Hydronephrosis
	35	27*	269	3- 8-35	3-13-35	5 days	Left ureter perforated with suture No. 1. Peritonitis	Urinary leakage
	36	28	279	3-14-35	5- 4-35	1 mo. and 20 days	Pyonephrosis	At time of operation the right ureter was perforated by suture No. 1 and then ligated purposely
	37	29	275	3-14-35	3-20-35	6 days	Cause undetermined	Good transplant
	38	30	321	4- 4-35	6-21-35	2 mos.	Bilateral pyonephrosis	
	39	31	338	4-11-35	8- 2-35	4 mos.	Left pyonephrosis. Slight hydronephrosis on right	
	40	32	327	4-18-35	4-21-35	3 days	Sepsis from infection of abdominal wound	Infection at site of implant. No peritonitis
	41	33*	342	4-25-35	4-30-35	5 days	Male, voided during operation, contaminating the wound. Peritonitis	Leakage on left
Submucosal Fold method (Fig. 6)	42	1	239	1- 4-35	4- 2-35	3 mos.	Killed	Marked left hydronephrosis, slight on right
	43	2	489	1- 8-35	1-15-35	7 days	Infection of wound. Uremia	No peritonitis. Hydronephrosis
	44	3	246	1- 8-35	2- 9-35	1 mo.	Right pyonephrosis. Infection of wound	No peritonitis
	45	4	263	1-16-35	1-21-35	5 days	Infection at site of implant. Acute pyelonephritis. Infection of wound	No leakage
	46	5	242	1-16-35	2- 9-35	24 days	Right, pyonephrosis. Left, good. Moderate infection of abdominal wound	No peritonitis
Muscularis Flap method (Fig. 7)	47	1	309	2- 1-34	2- 5-34	4 days	Evisceration	
	48	2*	105	7-31-34	8- 3-34	4 days	Infection of abdominal wound. Peritonitis. Right ureter sloughed out	
Higgins-Coffey method (Fig. 8)	49	1	265	(1) 1-31-35 (2) 2-13-35	2-26-35	13 days	Acute pyelonephritis (bilateral). Pneumonia	At the second operation there was found to be no drainage into the bowel on the right. This ureter was re-implanted by the 7 suture method
	50	2†	43	(Right only) 2-30-34	9-18-34	7 mos.	Killed	Well marked hydronephrosis
	51	3*	268	1-31-35 2nd stage not done	2-28-35	28 days	Infection of wound with abscess perforating into abdominal cavity, producing peritonitis	Ureters and kidneys good
	52	4*	277	(1) 2-8-35 (2) 3-8-35	3-15-35	5 wks.	Moderate infection of wound. Early peritonitis, right pyonephrosis	
	53	5	278	(1) 2-8-35 (2) 3-8-35	6- 1-35	3 mos.	Bilateral hydronephrosis	

*Died of peritonitis.
†Coffey method No. III on right. Left ureter was not implanted.

tis (serial numbers 2, 3, 4, 5, 10, 17, 29, 41, and 48, Table II). In 3 of these the fecal leakage resulted from a slight necrosis of the bowel at the site of implantation and in 3 instances the sutures had failed to hold and the ureteral ends had slipped out of the bowel entirely. All 4 dogs in which ureters were implanted directly (Fig. 1), rather than obliquely by a submucous route, died of peritonitis. In 3 of these there was gross leakage, in the fourth (No. 1), an abscess at the site of the right implant. Aside from the value of a submucous valve in the prevention of ascending infection, an oblique insertion of the ureter undoubtedly secures a tighter anastomosis and lessens the danger of leakage and peritonitis. The penetration of the lumen of the ureter by a suture caused urinary leakage in

1 dog (serial No. 27) which died of peritonitis. Ten of the 13 instances of peritonitis, therefore, resulted from leakage (of feces in 9 and of urine in 1).

C. Infection of the abdominal wound. Successful uretero-intestinal implantation in dogs is much more difficult than in man mainly because the ureter of the dog is smaller and has a much thinner wall. In addition, infection of the abdominal wound occurs frequently in dogs in spite of strict asepsis. This infection comes from contamination of the wound from the inside when the bowel is opened and from the outside (skin) at the time of or after closure. A sterile dressing was not applied. Twenty-three of the 53 dogs had more or less severe infection of the abdominal wound, and all died; 4 of evisceration, 8 of peritonitis, 9 of acute pyelonephritis, and 1 each of sepsis and pneumonia. Two of the 5 dogs which were operated on by Higgins' method died of peritonitis; in 1, an abscess in the wound ruptured into the peritoneum after 28 days, producing peritonitis, and the other died of peritonitis as a result apparently of contamination from the outside at the time the second stage of the operation was carried out.

D. Infection at the site of implantation. This may present as a localized inflammation, as part of a generalized peritonitis, or as a walled-off abscess. The last condition occurred three times and was unassociated with peritonitis in 2 instances. Had these 2 dogs lived long enough, the local abscesses might have ruptured into the peritoneal cavity. Undoubtedly this complication is the gravest of the dangers from contemporary contamination. Infection about the ureter as it enters the bowel may produce peritonitis not only by direct extension but indirectly by causing localized necrosis of the bowel or ureter and the formation of a fistulous tract. Direct extension seems to have been the cause of peritonitis in 2 dogs (Nos. 45 and 52). The relation of inflammation arising from contamination and of necrosis resulting from suturing, to the production of the localized sloughing which permitted leakage of the contents of the bowel, is uncertain. Undoubtedly, both are important factors.

SUMMARY

1. Peritonitis rarely occurs as a result of contamination with the contents of the bowel or with urine at the time of operation when the obvious precautions are followed.

2. Leakage from the bowel or the ureters after operation is the common cause of peritonitis.

a. Leakage occurs when the anastomosis is faulty and the ureter has not been sutured securely into the opening of the intestine. (An oblique submucous insertion of the ureter is much safer than direct insertion.)

b. Leakage occurs when anchoring sutures tear or slough out. (Sutures through serous and muscular layers of the bowel are insecure. The only safe layer for suturing is the submucosa, the use of which carries the greater risk of penetration of the lumen.)

c. Leakage occurs when a suture punctures the bowel (fecal fistula) or the ureter (urinary fistula).

d. Leakage occurs with necrosis of a portion of the intestine or of the transmural portion of the ureter. (The blood supply of the bowel or ureter must not be tied off by sutures or impaired by too great constriction, which may occur by suturing in layers.)

3. Infection of the abdominal wound from contamination at the time of the operation is more imminent than peritonitis. Abscesses in the abdominal wall may rupture to the inside and produce peritonitis. (The incision should be walled off more securely than the intestines are packed off, and gloves, drapes, and instruments should be changed before closure is carried out.)

4. Implantation, by any method which requires that the bowel be opened at the time, carries the considerable risk of localized inflammation both of the bowel and of the ureter. A localized peritonitis may clear up or become general. A local abscess may be absorbed or it may rupture into the cavity and then produce peritonitis. A periureteritis may produce urinary obstruction or the infection may ascend to the kidney. Localized inflammation may lead to anemic necrosis of the bowel or ureter, which will permit leakage, and peritonitis will be the result. Inflammation at the site of implantation may result

from temporary leakage after operation, and probably this is the most frequent cause. (The operative technique must prevent local contamination and secure a water-tight anastomosis.)

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THE COURSE OF SINGLE MYELOMA OF BONE

A Report of Twenty Cases[1]

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THE question as to whether or not myeloma of bone is a true tumor or a generalized disease of the myeloid system has not been settled. Most authors incline to the view that these lesions must be classified as true tumors.

The term "multiple myeloma" has arisen because these tumors spread very early, and cases are usually observed only in those stages in which the disease is already generalized. In order to support the opinion that myeloma is a true tumor, following the course characteristic of tumors, the observation of cases with a solitary bone lesion with or without subsequent spread of the disease is very important. Geschickter and Copeland state in their book as late as 1931: "In only 5 cases (Wallgren, Schmorl, Morax and Geschickter) has the disease been found in a single focus, and in all of these cases autopsy was not performed, although thorough roentgen-ray studies were made in some."

This communication contains cases of myeloma collected from the literature which were proved either by necropsy or roentgen-ray findings to be single myeloma with or without subsequent spread of the disease. In addition, the Bone Registry of the American College of Surgeons was studied and similar cases from this registry are included in this report. It was necessary to eliminate from the literature those cases diagnosed as single myeloma in which the proof was not based upon roentgen or necropsy findings. Among the cases to which Geschickter and Copeland refer, we found it necessary to eliminate the cases of Morax and Schmorl which were not definitely single cases at the first observation. The case reported by Ewald, which is considered by some to be one of single myeloma, we found necessary to eliminate because of the indefinite histological findings.

We have collected from the literature 12 cases which, in our opinion, meet the requirements mentioned. We have added to this group 5 cases which were found in a group of 75 registered as myeloma in the Bone Registry of the American College of Surgeons. One additional single myeloma (Case 13) is added. Cases 19 and 20 are presented as problems in radiological differential diagnosis.

Case 1. Zdansky reports the case of a woman, age 68, who complained of joint pains of 1 year's duration. The patient had an intense albuminuria, secondary anemia, nephrosis, and thrombopenic purpura. Pain in the left leg was severe.

X-ray reports. In the upper third of the left femur there was an area of rarefaction, irregular in outline and 8 centimeters in length. The cortex was thin and in some places completely destroyed. "In other parts of the skeleton, lesions were not found roentgenologically." A few days after these roentgenograms were taken, a spontaneous fracture of the femur occurred. (The patient died shortly thereafter from heart disease.)

Necropsy. An amyloidosis of the heart and kidneys with shrinking of the kidneys was found. A plasmocytoma was found at the site of the fracture of the left femur. The central part of the tumor was destroyed by necrosis and hemorrhage. The yellow marrow was partly replaced by red marrow in the long bones. Histologically, sections of the tumor showed plasma cells with many mitoses. The histological diagnosis was plasmocytoma (Institut Maresch, Vienna).

The original communication presents a photograph of the femur with pathological fracture.

This case presents a single tumor of the femur diagnosed histologically as plasmocytoma; roentgenologically no other lesions could be found throughout the skeleton. Concerning Bence-Jones protein, nothing is mentioned in the report.

Case 2. Geschickter reports the case of a woman, age 45, who complained of pain in the upper third of the left thigh of 2 months' duration.

Examination October, 1929 (Dr. Bloodgood). Clinically, the patient had pain only in the left thigh. Roentgenograms of the left femur revealed an area of bone destruction in the upper portion of the shaft at the site of the nutrient artery, extending from the intertrochanteric line to the beginning of the middle third of the femur. Cortical bone was intact without signs of periosteal destruction or reaction. Roentgenograms of the other long bones, the pelvis, spine, ribs, and skull, were negative.

[1] From the Tumor Clinic of the Michael Reese Hospital, Chicago.

Exploratory operation by Dr. Bloodgood. Unusual vascularity and hemorrhage were encountered under the periosteum. The cavity seen in the X-ray film was cauterized. A frozen section showed the tumor to be composed of sheets of cells resembling plasma cells. Permanent sections confirmed the diagnosis of myeloma of the plasma cell type.

Pathological fracture occurred shortly after operation.

This case presents a plasma cell myeloma of the femur diagnosed by biopsy. X-ray examination at the time of operation revealed no other lesions of bone. Bence-Jones protein was not found.

CASE 3. Wallgren reports the case of a woman, age 41, who in 1918 pulled two small fragments of bone from the posterior portion of the right upper jaw. A few weeks later she observed a small, hard nodule at the site of the right upper second molar tooth. On examination, the tumor was fluctuant. There was a chronic tuberculosis of the right apex. On X-ray examination there was found a defect in the alveolar process. Skeletal X-rays revealed no other myelomas. The urine contained Bence-Jones protein.

The tumor was resected. Histologically, it was composed of masses of small cells, alveolar in structure with many blood vessels containing large endothelial cells. These vessels contained myeloma cells of the plasma cell type. The histological picture was similar to other cases of myelomas reported by Wallgren.

The case presents a tumor of the right upper jaw. Histologically, plasma cell myeloma could be diagnosed from plasma cells found in the vessels. These were of the same type as in other cases of multiple myeloma reported by the same author. Bence-Jones protein was found in the urine. Although the author is unable to arrive at the definite conclusion that this case is one of single myeloma, the presence of Bence-Jones protein with a single lesion and the histological finding of plasma cells support the assumption that this case is a single myeloma of the plasma cell type.

CASE 4. Rogers presents the case of a man, age 34, who sustained a fracture of the right femur in November, 1927. In December, 1927, a second injury occurred at the same site following which swelling of the limb occurred.

Examination June 21, 1928 (Bristol General Hospital). There was a large fusiform swelling on the anterior inner aspect of the right thigh, firmly attached to bone and of seeming solid consistency. X-ray examination revealed a honey-combed appearance in the tumor mass and a rarefaction of bone extending above and below the site of the former fracture.

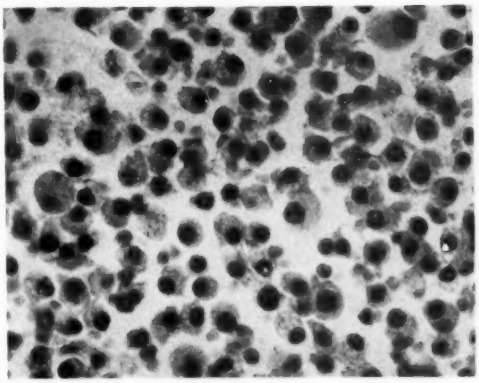

Fig. 1. Solitary plasma cell myeloma of the femur. (Case 10. Photomicrograph taken from the original section of the Bone Registry No. 1438.)

First operation June 22, 1928. Curettage. The tissue removed was firm, grayish-white in appearance, and contained many areas of hemorrhage. Microscopically, the tissue was composed of discrete polyhedral cells. The pathological diagnosis was plasma cell myeloma.

X-ray examination of the skeleton failed to disclose other foci of tumor formation. The urine contained no Bence-Jones protein.

July 3, 1928, radium needles were inserted in the cavity (150 mgm.) and removed on the following day.

The discharge of purulent fluid necessitated a second operation on November 27, 1928, with insertion of 140 milligram radium needles for 2 days and a third operation on January 8, 1929, at which time the cavity was filled with plaster of Paris. On February 5, 1929, amputation through the upper third of the thigh was performed.

According to a personal note received from the surgeon who performed the operation in this case (Professor Hey Groves), the patient was last seen on May 9, 1932, at which time he was in good health and without signs of recurrence or generalization.

This case presents a single tumor in the femur which was first revealed following a fracture. Histologically, the tumor proved to be plasma cell myeloma. No other bones were involved. Bence-Jones protein could not be demonstrated in the urine. Following three curettages and final amputation, the patient has been well at least 4 years since the diagnosis of myeloma. Amputation was performed 8 months after the original diagnosis.

Fig. 2. Tumor of upper end of right femur at time of first observation. (Case 14. Bone Registry No. 710.)

CASE 5. Shaw reports the case of a man, age 29, who sustained a fracture of the right humerus in the middle third of the shaft. One week after the fracture, a roentgenogram of the humerus revealed absorption and reticulation of bone at the site of fracture suggesting a central medullary tumor. X-ray examination of all bones failed to reveal other lesions. The humerus was exposed at operation and a soft medullary tumor at the site of fracture was removed by curettage. Microscopic examination of the tissue removed at operation revealed an extremely cellular tumor with extensive hemorrhage. No multinucleated giant cells were present. Pathological diagnosis was plasma cell myeloma. Several examinations of the urine after operation failed to show Bence-Jones protein. Twelve months after fracture there was good union of bone and no evidence of recurrence of tumor.

In a personal communication received from the author, it is stated that the patient was last seen in 1931, at which time there was no evidence of local recurrence or generalized myelomatosis.

CASE 6. Charbonnier and Mermod report the case of a woman, age 62, who complained of pain in the left hip. In August, 1932, the patient sustained a fracture of the upper third of the left femur following slight trauma. Examination at this time disclosed a fracture of the upper third of the left femur. The bone was rarefied and the cortex irregularly thin and cystic. X-ray examinaion of the femur 1 month later showed progress of the disease.

November, 1932, curettage was done. Microscopic examination showed tissue which consisted entirely of plasma cells. The histological diagnosis was myeloma. An instructive photomicrograph is included.

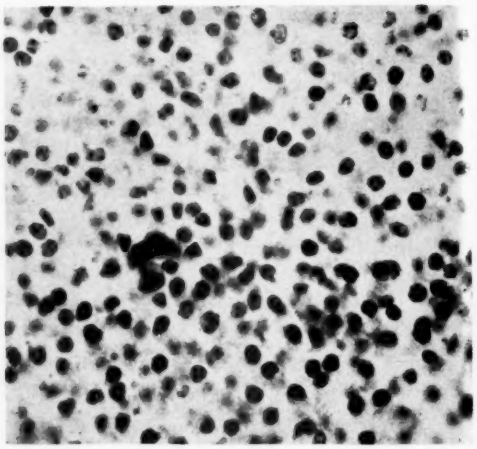

Fig. 3. Photomicrograph. Plasma cell myeloma. Biopsy of the primary lesion of femur. (Case 14. Bone Registry No. 710.)

Bence-Jones protein was not found in the urine. Following the operation, a fistula occurred in the scar and a short time later a sacral tumor appeared which perforated into the rectum. The patient became cachectic and on January 15, 1933, died of cachexia.

Necropsy (Askanazy) did not show other skeletal tumors in spite of a very careful examination (skull, ribs, sternum, pelvis, spine, long tubular bones of the extremities). The histological postmortem diagnosis was solitary myeloma of the plasmocytoma type.

The anatomical findings in this case are extensively reported by Rutishauser. This author calls special attention to the infiltrative character of the tumor. For this reason, Askanazy proposes the term myelosarcoma for this case.

This case presents a solitary tumor in the upper third of the femur which was diagnosed histologically as plasma cell myeloma. Bence-Jones protein was not present. No other parts of the skeleton were involved.

The striking feature of this case is the malignant course and rapid growth of the solitary tumor. From the reproduction of some of the X-ray films, one might diagnose osteogenic sarcoma. The entire course of the disease from the first diagnosis to death was only 6 months.

CASE 7. Walthard presents the case of a man, age 55, who in August, 1922, noted pain in the back of the neck. In May, 1923, the patient experienced difficulty in walking, with symptoms denoting compression of the spinal cord below the first dorsal segment.

Fig. 4. X-ray of skull December 31, 1923. Made at time of original observation of the tumor of the right femur. No visible lesion in the skull. (Case 14. Bone Registry No. 710.)

Fig. 5. X-ray of skull September 24, 1926, at the time of generalization of the disease. Three years after original observation of primary tumor. (Case 14. Bone Registry No. 710.)

In June, 1928, a laminectomy was performed and the patient died after operation.

At necropsy destructive lesions of the first thoracic vertebra and the seventh cervical vertebra were found. The tissue was grayish-red and hemorrhagic. The histological findings revealed plasmocytoma, the cells of which contained the typical spoke-like nuclei.

Bence-Jones protein was not reported. There were no lesions in the other bones.

Fig. 6. Lesion of the femur 3 years after original observation of myeloma. (Case 14. Bone Registry No. 710.)

This case presents a tumor which had destroyed two vertebræ, and which was diagnosed microscopically (Hedinger) as plasmocytoma. The patient died after operation. The invading character of this tumor is noteworthy. A photomicrograph is included.

CASE 8. Mathias presents the case of a man, age 65, who had observed a slowly growing tumor of the right parietal area. The tumor was widely excised. Histological examination showed a myeloma with cell structure of plasmocytoma. The patient had

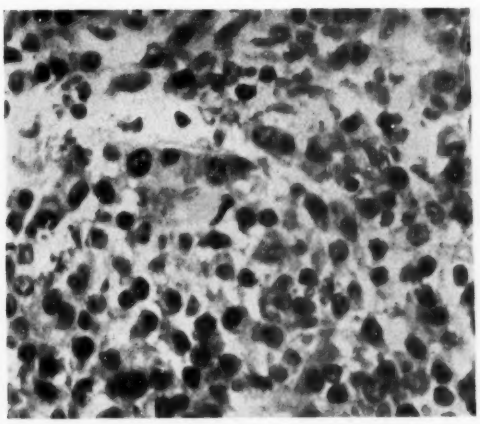

Fig. 7. Plasma cell myeloma of humerus. (Case 15. Bone Registry No. 1597.)

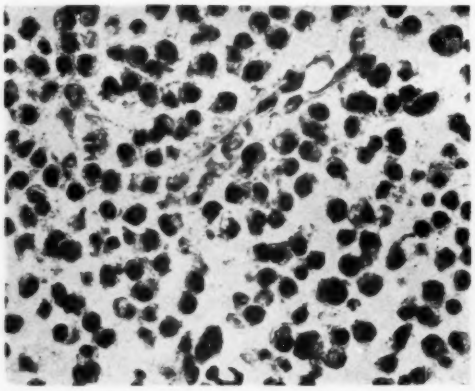

Fig. 8. Photomicrograph. Plasma cell myeloma of the ilium. (Case 16. Bone Registry No. 1148.)

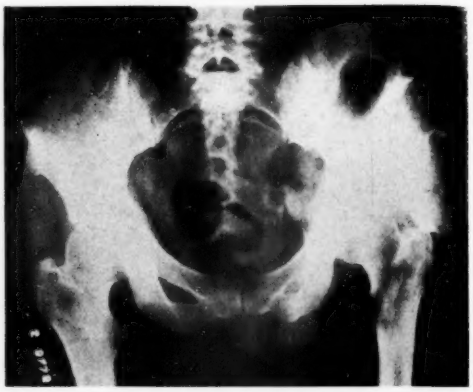

Fig. 8a. Myeloma of the ilium with roentgenographic appearance of giant cell tumor. (Case 16. Bone Registry No. 1148.)

been free of disease 18 months at the time of the report. During the observed course of the disease, no other bone involvements had been noted. Bence-Jones protein was not found in the urine.

CASE 9. Cabot presents the case of a man, age 33, who was admitted to the Massachusetts General Hospital acutely ill. The patient had neurologic signs of compression of the spinal cord at the level of the fourth thoracic vertebra.

Laminectomy was performed, at which time a grayish mass was found at the level of the fourth dorsal vertebra which did not invade the dura. The patient subsequently died.

The patient was found to have infarcts and abscesses of the right lung with hemorrhagic cystitis. Primary myeloma of the bone marrow in the fourth dorsal vertebra was found. At the post-mortem examination no tumor was found anywhere else in the body.

Regarding the histology of this tumor, Dr. Tracy B. Mallory states: "I think, however, there is no question but the tumor has to be classified in the general group of myeloma. I mean by that simply a primary tumor of the bone marrow which is not the typical plasma cell myeloma and we are not able to decide which of the various other types it is. In some areas it shows cells suggesting plasma cells, in other areas extraordinary numbers of multinucleated giant cells suggesting strongly a tumor of megakaryocytes."

CASE 10. Bone Registry of the American College of Surgeons. Case Number 1438.

Fig. 9. Destructive lesion of second lumbar vertebra. (Case 18. Bone Registry No. 1167.)

Fig. 10. Destructive lesion of second lumbar vertebra 6 years after Figure 9. Histologically the lesion was plasma cell myeloma. (Case 18. Bone Registry No. 1167.)

Fig. 11. Destructive lesion of the eighth thoracic vertebra. Microscopically plasma cell myeloma. (Case 19. Michael Reese Hospital, Tumor Clinic, No. 2147.)

Harding and Kimball report the case of a man, age 60, who in January, 1930, complained of a dull aching pain in the region of the left hip which radiated down to the knee. In June, 1930, pathological fracture of the femur at the level of the lesser trochanter was found. The radiographic appearance was that of a purely osteolytic lesion and was confined to the region of the fracture.

Examination July 19, 1931 (Los Angeles County General Hospital). Radiographic examination of the entire skeleton showed the lesion to be limited to the left femur. At the level of the lesser trochanter there was an area of rarefaction with a widening of the adjacent shaft. The medullary cavity was more extensively involved than the cortex.

The urine was negative for Bence-Jones protein.

In September, 1931, a disarticulation of the leg at the hip joint was performed, and the patient died in surgical shock.

Examination of the removed extremity showed a tumor 7 centimeters in diameter occupying the medullary cavity which had produced a destruction of the cortex of the femur and had invaded the muscles of the thigh. The microscopic picture (Fig. 1) was characteristic of plasma cell myeloma. The pathological diagnosis was plasmocytoma of the femur.

Careful examination of the other bones at necropsy failed to disclose other foci of tumor.

This case presents a solitary plasmocytoma of the femur with pathological fracture. The patient died in surgical shock after disarticulation 15 months after the lesion was first observed roentgenologically and 20 months after the first subjective symptoms had developed. Examination of the skeleton both by X-rays during life and at necropsy failed to show other lesions. The urine contained no Bence-Jones protein.

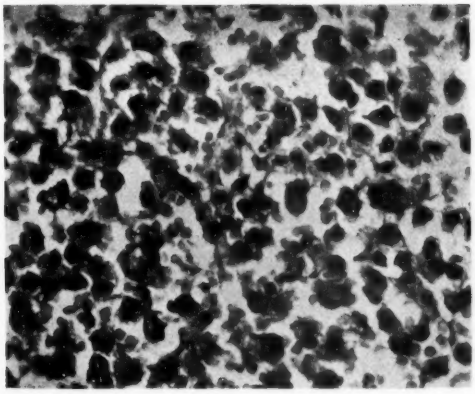

Fig. 12. Plasma cell myeloma. (Case 19. Michael Reese Hospital, Tumor Clinic No. 2147.)

A remarkable feature in this case is the invasive character of the tumor. The case is accepted by the Bone Registry of the American College of Surgeons as plasma cell myeloma.

CASE 11. Bloodgood reports the case of an adult male who had sustained trauma to the right shoulder. Thirteen months later swelling appeared in the outer third of the clavicle.

X-ray examination demonstrated a uniform expansion of the medullary cavity of the outer third of the clavicle in which only a very thin shell of bone was preserved. The X-ray film revealed a lesion resembling a bone cyst or a giant cell tumor. No other skeletal X-rays were taken prior to operation.

No examination of the urine for Bence-Jones protein was made before the operation.

In view of the rapid growth and very thin bony shell, resection was performed. The tumor consisted of a whitish mucoid material with hemorrhagic areas. Frozen sections gave the appearance of round cell sarcoma and contained cells characteristic of myeloma.

After operation, Bence-Jones protein was found in the urine.

X-ray studies of the other bones of the skeleton were negative until some 2 months after operation, at which time a second bone focus was found in one of the ribs.

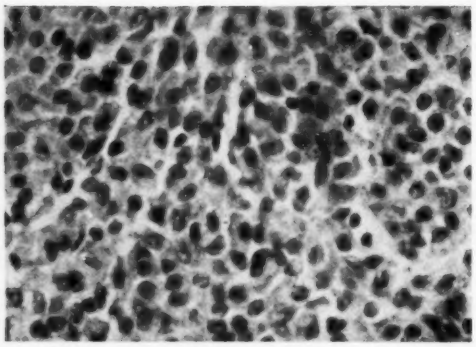

Fig. 13. Plasma cell myeloma of the femur. (Case 20. Bone Registry No. 1101.)

This case presents a tumor in the outer third of the right clavicle histologically diagnosed as myeloma. Skeletal X-ray films showed no other lesions until 2 months after operation. The urine contained Bence-Jones protein in large quantities even before generalization of the disease was observed.

CASE 12. Peyton presents the case of a man, age 49, who began to have pain in the region of the xyphoid process radiating across the upper abdomen 1 year prior to the first examination. Weakness developed in both legs 4 months prior to examination.

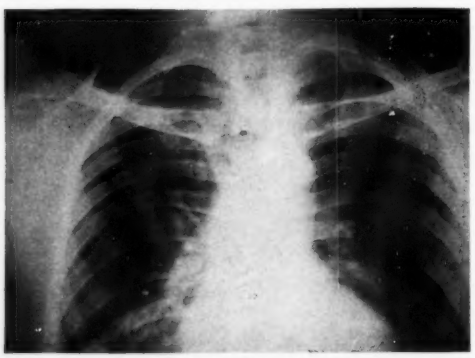

Fig. 15. As a further demonstration of the difficulties encountered in the roentgenological diagnosis of myeloma, we present an X-ray film of the chest taken of a patient with typical, multiple generalized myelomas proved by biopsy. Bence-Jones protein was present in the urine. This film reveals typical discrete punched out lesions in the ribs as well as a lesion in the outer third of the right clavicle which, if seen by itself, might lead one to the diagnosis of giant cell tumor of the clavicle from the roentgenological appearance alone. (This picture was obtained through the courtesy of the Edward Hines Hospital of the United States Veterans' Facility, Hines, Illinois.)

Fig. 14. Roentgenogram of the right femur showing bone destruction with cortical expansion. Roentgenological diagnosis, giant cell tumor. Histological diagnosis, plasma cell myeloma. (Case 20. Bone Registry No. 1101.)

Examination July, 1930. The X-ray films showed the sixth thoracic vertebra to be compressed and rarefied and the intervertebral disc between the fifth and sixth thoracic vertebræ to be almost obliterated. X-ray films of the lungs and ribs were negative. The urine was not tested for Bence-Jones protein.

Treatment. On September 3, 1930, laminectomy was done. The sixth thoracic vertebra and the head and neck of the sixth rib were replaced by tumor. The dura and cord proper were not invaded, although surrounded and compressed by tumor. Eleven radium needles (65 milligrams total) were inserted into the tumor mass and left in place for 20 hours, giving a total dose of 1300 milligram hours. Filtration of 0.5 millimeter nickel steel was used.

Microscopic examination of the tissue removed at operation revealed small round cells with hyperchromatic nuclei and with an occasional mitotic figure. The pathological report was plasma cell myeloma.

After operation, the patient received external X-ray therapy in four treatments over a 6 day period. Through an anterior and a posterior portal, the patient received 132 per cent skin erythema dose to each portal with 200 kilovolts, 1 millimeter copper + 1 millimeter aluminum, at a skin target distance of 50 centimeters. One year later a second series of X-ray treatments was given.

The patient could walk following operation. Skeletal X-ray examination in March, 1932, did not reveal additional lesions. The urine at this time con-

tained Bence-Jones protein. In February, 1934, the patient was still living but had generalized metastases of the skeleton. The patient died in March, 1934.[1]

This case presents a primary myeloma of the vertebra with no other skeletal involvement over a period of 19 months. Generalized myeloma followed the primary tumor. The urine was not examined for Bence-Jones protein in the early stages. After the disease had become generalized, Bence-Jones protein was present.

CASE 13.[2] This patient was a woman, age 38, who received an injury to the left parietal bone in October, 1928. In December, 1928, she observed a soft swelling over this area which was not tender or painful.

In March, 1929, the patient was examined at the Mayo Clinic. At this time a large, cranial defect was found in the left parietal bone, replaced by a soft pulsating mass. No other rarefactions were noted in the skull, spine, ribs, chest, or sternum. The blood count was normal; the Wassermann, negative. Blood calcium was 9.9 milligrams per cent. The patient received X-ray therapy over the tumor.

In April, 1929, the tumor had disappeared. The patient complained of pain in the left shoulder. Skeletal X-ray films were still negative. Bence-Jones protein was present.

In May, 1929, skeletal X-ray films revealed numerous punched out areas throughout the skull. Bence-Jones protein was again present. The patient received additional X-ray therapy.

In January, 1930, the patient sustained a fracture of the left humerus which healed in 6 weeks. At this time hemoglobin was 29 per cent. The patient complained of pain in the joints, chest, and extremities.

In March, 1931, the patient was admitted to University Hospital (Minnesota). Skeletal X-ray examination revealed many areas of rarefaction with pathological fractures of several of the ribs and of the pubes. Roentgenological findings were characteristic of multiple myeloma. The urine contained large quantities of Bence-Jones protein. The patient died on March 4, 1931, of intestinal obstruction after an appendectomy had been performed.

Postmortem (abdominal only). The abdomen contained about 500 cubic centimeters of bloody fluid. No evidence of mechanical obstruction was found. The lower ribs were thickened and were the site of several fractures. The iliac bones were soft and friable. Marrow obtained from the ribs and iliac bones gave the characteristic appearance of plasma cell myeloma.

The first observation of this case 4 months after the onset of the symptoms revealed a lesion in the left parietal bone only. One month later, skeletal X-ray films revealed no other lesions. At this time Bence-Jones protein was present. One month later (2 months after the first observation and 6 months after the appearance of the primary tumor) generalized metastases to the skull could be demonstrated. The patient lived 2 years and 4 months after the diagnosis of the primary lesion and 1 year and 9 months after generalization occurred. Histologically, plasma cell myeloma was found at necropsy.

CASE 14. Bone Registry of American College of Surgeons. Case Number 710.

Patient was a male, age 56, who at the age of 21 was injured in a railroad accident. Paralysis of the lower extremities was present following this accident. The patient recovered and was apparently well until the age of 56, at which time there was slight pain in the right upper thigh in the region of the greater trochanter. One month later X-ray films showed a bone tumor of the upper end of the right femur (Fig. 2[3]), intramedullary in position. The lesion was considered to be a giant cell tumor. X-ray examination of the other bones revealed no further lesions.

The urine contained no Bence-Jones protein.

In January, 1924, curettage was done, at which time fracture of the femur occurred. The extremity was placed in Buck's extension. Microscopic examination of tissue revealed typical plasma cells in various stages of mitosis. Diagnosis was myeloma of the plasma cell type (Dr. A. A. Eggston, Dr. F. Parker, Jr., Dr. F. B. Mallory, and Dr. J. Ewing), (Fig. 3).

In December, 1925, the patient was in excellent general condition. In September, 1926, generalized metastases were observed (Fig. 5[3]). The patient died in 1926 shortly after the accompanying photographs (Figs. 5 and 6[3]) were made. Bence-Jones protein was found in the urine prior to death.

This case presents a single myeloma of the right femur diagnosed microscopically as plasma cell myeloma. The exact interval between the diagnosis of the primary tumor and the later generalization cannot be determined. Two years after the discovery of the primary tumor, the patient was still in excellent health. He died 3 years after the original diagnosis had been made. Bence-Jones protein, which was not found in the early stages of the disease, was demonstrated prior to death.

CASE 15. Bone Registry of American College of Surgeons. Case Number 1597. Patient was a man, age 57, who in May, 1932, sustained trauma to right shoulder with fracture.

[1] Information regarding the subsequent course of the disease was received from Dr. W. T. Peyton.

[2] This case was reported to us in a personal communication from Dr. W. T. Peyton.

[3] X-ray films reproduced here were obtained through the courtesy of Dr. Joseph E. J. King.

In December, 1932, X-ray examination (Out Patient Department of the Vanderbilt University Hospital, Nashville) showed a destructive lesion in the proximal portion of the right humerus. A complete destruction was found just below the head of the humerus with pathological fracture and extension into the soft tissues. The impression was that of a sarcoma of the humerus.

In May, 1933, the presence of Bence-Jones protein was questionable at first examination. On repeated examinations Bence-Jones protein was absent. X-ray examination at this time revealed a complete destruction of the medulla and cortex and invasion of the soft tissues. X-ray examination of the skull, pelvis, and chest revealed no other lesions.

A resection of the proximal end of the humerus was done. At operation the tumor seemed to be entirely enclosed by normal periosteum. The tumor tissue was composed of dark red, friable material which, microscopically, was composed of closely packed cells resembling plasma cells. Mitotic figures were common. No giant cells or no new bone formation could be seen (Fig. 7). The original pathological diagnosis was myeloma, although not a typical plasma cell type. Subsequent diagnosis of plasma cell myeloma was made by Drs. Crowell, Hartman, Morton, Warren, Lebowitz, and Simmons.

In September, 1933,[1] numerous small areas of increased penetration through many of the ribs were found by X-ray examination. In May, 1934, X-ray examination revealed increased penetration over the wing of the left ilium and near the acetabulum on the right. The right scapula and many of the ribs showed small areas of increased penetration suggestive of multiple myeloma. In October, 1934, both clavicles and many of the ribs showed areas of increased penetration varying in size.

Bence-Jones protein was found in the urine for the first time.

In November, 1934, the patient received X-ray therapy (total 1500 r).

The patient died in April, 1935.

This is a case report of a single myeloma of the humerus associated with pathological fracture. At the original examination no other bones were involved, and the urine was negative for Bence-Jones protein. The first signs of generalization were found 10 months after the diagnosis of the primary lesion was made, and 17 months after the first fracture occurred. Bence-Jones protein was found in the urine for the first time 23 months after the first diagnosis.

CASE 16. Bone Registry of the American College of Surgeons. Case Number 1148.

This patient was a woman, age 39, who was admitted to St. Michael's Hospital in Toronto. Two years prior to first examination, the patient developed pain in the left hip which was diagnosed as sciatica. In January, 1928, there was pain radiating from the left hip to the left knee upon movement. Upon admission to the hospital there was a round, firm swelling over the left anterior superior spine of the ilium, and marked atrophy of the muscles of the left lower extremity.

In August, 1928, a biopsy of the tumor was done (Fig. 8). The pathological diagnosis was plasma cell tumor (myeloma). Bence-Jones protein was found in the urine at this time. Subsequent X-ray examination of the skeleton did not reveal other lesions. X-ray examination of the left ilium showed a large tumor of the ala, having the radiographic appearance of a giant cell tumor (Fig. 8a).[2]

In February, 1929, the patient received X-ray therapy.

In June, 1930, the patient died.

At necropsy myeloma of the left ilium was found. In addition there were pulmonary abscesses and a chronic nephritis. Gross examination of the skeleton at necropsy revealed no evidence of tumors in other bones.

This case presents a single myeloma of the left iliac bone. The sections show a myeloma of the plasma cell type (Drs. Crowell, Codman, Simmons, Stewart, Copeland, and Magner). Neither X-ray examination during the life of the patient nor gross examination at necropsy revealed any evidence of tumors in other bones. Bence-Jones protein was positive in the urine in a comparatively early stage. The patient died with symptoms referable to a chronic nephritis. Unfortunately, the clinical analysis from the point of view of the nephropathy does not indicate whether the kidney changes are referable to the metabolic disturbances associated with Bence-Jones proteinuria (myelomatous nephrotic contracted kidney). From the literature and in our own experience, typical changes in the kidneys have been observed only in the generalized state of the disease. Therefore, this case would be very important from the point of view of the relation of the metabolic disturbances and the extension of the bone disease. More clinical and pathological data in regard to the kidney pathology in this case would be pertinent to the relation between Bence-Jones proteinurea, kidney changes, and the stage of generalization of the disease.

[1] The following information was obtained through the courtesy of Dr. B. M. Weinstein.

[2] This X-ray film was obtained through the courtesy of the X-ray Department of the St. Michael's Hospital, Toronto, Canada.

CASE 17. Bone Registry of American College of Surgeons. Case Number 1195.

A man, age 58, was admitted on the Genito-Urinary Service of the Massachusetts General Hospital with prostatic obstruction. X-ray examination taken on this occasion revealed a large area of diminished density with trabeculation in the right ilium. Biopsy showed plasma cell myeloma.

In March, 1931, general skeletal roentgenograms were negative. X-ray therapy was given.

In May, 1931, general condition was excellent. X-ray examination of the pelvis showed some filling in of new bone and expansion of the process.

In August, 1932, the condition remained the same.

This case presents a single plasma cell myeloma of the right ilium. (Drs. Crowell, Codman, Stewart, Simmons, Broders, Meyerding, Brooks). There were no signs of involvement of other bones. Bence-Jones protein was not reported. The patient was well 20 months after the first observation of the tumor.

CASE 18. American College of Surgeons Bone Registry. Case Number 1167.

A Negro man, age 52, was admitted to the Massachusetts General Hospital in December, 1924. His chief complaint was pain in the right leg following an injury. The X-ray examination revealed a destructive lesion of the body of the second lumbar vertebra. The diagnosis was giant cell tumor.

In August, 1930, the condition of the patient was more acute. At this time there was vertebral compression. The patient was given X-ray therapy without noted improvement.

In December, 1930, a stabilizing operation was done. Microscopic diagnosis of tissue removed at this time was plasma cell myeloma.

Complete skeletal X-ray films taken later showed no other bone involvement. The urine showed no Bence-Jones protein.

In September, 1932, the patient's general condition was good, but the disease had extended to adjacent vertebræ.

In August, 1934, the condition remained unchanged.

This is a case report of a single myeloma of the vertebra which was diagnosed as plasma cell myeloma (Drs. Crowell, Ewing, Stewart, Simmons, Codman, Hartwell, Hartman, and Broders). The skeletal X-ray films revealed no other foci of bone involvement 6 years after the first observation. Bence-Jones protein was not found in the urine. Eight years after the original observation the process had extended to adjacent vertebræ. At the patient's last examination the disease had been observed over a period of 10 years, and at that time was still present in the original vertebra and the adjacent vertebræ.

CASE 19. A Negro man, age 56, in December, 1934, noted the onset of sharp, shooting pains radiating from the perineum down both lower extremities. Progressive weakness and stiffness of both lower limbs developed until June, 1935, when he became completely bedridden. In June, 1935, he was admitted to the Michael Reese Hospital, at which time he had a spastic paraplegia. There was marked adductor spasm. Loss of cutaneous sensation was found on the left side up to the level of the tenth thoracic segment, and on the right side to the twelfth thoracic segment. There was bilateral exhaustible ankle clonus. Knee and ankle jerks were bilaterally brisk and equal. There was a bilateral positive Babinsky. Proprioceptive sensation was present in feet and ankles. The cremasteric and abdominal reflexes were bilaterally absent. There was a positive Beevor's sign. The upper extremities and cranial nerves were normal.

A diagnosis of spinal cord neoplasm at the level of the ninth, tenth, and eleventh skin segments was made. The urine was not examined for Bence-Jones protein.

X-ray examination (Fig. 11) of the spine showed a rarefaction of the bone of the eighth thoracic vertebra. The bone outline was practically intact, but the general appearance was that of a destructive lesion of the eighth thoracic vertebra.

Operation by Dr. David Cleveland, June, 1935. A laminectomy was done over the fifth, sixth, and seventh vertebræ. Laminæ of the sixth and seventh vertebræ were softer than normal. The spinous processes of the sixth and seventh vertebræ were undermined by a soft, gelatinous reddish-brown tumor mass. The spinal cord was completely covered in the region of the fifth, sixth, and seventh thoracic vertebræ by this soft tumor tissue which extended completely around the cord and upward beneath the lamina of the fourth thoracic vertebra. Because of the widespread involvement, it was deemed surgically unwise to do more than decompression of the cord over this area. Microscopic examination of tissue removed at operation revealed a myeloma of small round cells with darkly staining eccentric nuclei. A diagnosis of plasma cell myeloma was made (Dr. Max Cutler), (Fig. 12).

X-ray examination of the skull, chest, and femora taken 6 weeks after operation revealed no evidence of other lesions of bone. In the left ilium there was a sharply outlined area of rarefaction about 0.5 centimeter in diameter, which was probably an early secondary focus.

The urine was repeatedly negative for Bence-Jones protein.

This case cannot be presented as one of single myeloma because X-ray films taken 6 weeks after operation revealed a questionable

TABLE OF CASES

Case Sex Age	Location of primary tumor	Bence-Jones protein		Time from onset of symptoms to 1st observation	Complete period of observation to time of case report	Time from primary tumor to death	Living	Treatment	Single or later generalized†	Remarks	Source of material
		Early stages	Later stages								
1 F 68	Femur (upper third)	?	?	1 yr.	Observed only short time (days)	Short time (days)			R S	Associated nephrosis with albuminuria, thrombopenic purpura, and secondary anemia	Zdansky
2 F 45	Femur (upper third)	o		2 mos.	?			Biopsy	R S	Postoperative pathological fracture	Geschickter
3 F 41	Maxilla	+		Few wks.	?			Resection	R S		Wallgren
4 M 34	Femur	o	o	7 mos.	4 yrs.		4 yrs. (not followed up longer)	Curettage, radium puncture amputation	R S	Pathological fracture. Radiographic appearance of giant cell tumor	Rogers
5 M 29	Humerus (middle)	o	o	1 wk.			9 yrs.	Curettage	R S	Pathological fracture	Shaw
6 F 62	Femur (upper third)	o	o	Several mos.	6 mos.	6 mos.		Curettage	N S	Pathological fracture. Malignant invasive tumor	Charbonnier and Mermod, Rutishauser
7 M 55	Vertebræ (7th cervical 1st thoracic)	?	?	10 mos				Laminectomy and curettage	N S	Invasive tumor. Patient died postoperatively	Walthard
8 M 65	Skull (parietal)	o	o	?	18 mos.		18 mos.	Excision	S		Mathias
9 M 32	Vertebra (4th thoracic)	?	?	6 wks.	?	?		Laminectomy	N S		Cabot—Heffron
10 M 60	Femur (upper third)	o	o	6 mos.	2 mos.	2 mos.		Disarticulation	RN S	Pathological fracture. Radiographic appearance of giant cell tumor	Harding—Kimball Bone Registry 1438
16 F 39	Ilium	+		2 yrs.	23 mos.	23 mos.		X-ray	RN S	Associated chronic nephritis. Radiographic appearance of giant cell tumor	Bone Registry 1148
17 M 58	Ilium	?	?		1 yr. 7 mos.		1 yr. 7 mos.	Biopsy	R S		Bone Registry 1195
18 M 52	Vertebra (2d lumbar)		o	?	10 yrs.		10 yrs.	X-ray, stabilizing operation	R S	Radiographic appearance of giant cell tumor	Bone Registry 1167
11 M adult	Clavicle (outer third)	++		13 mos.	2 mos.*	?		Resection	G	Radiographic appearance of giant cell tumor. One secondary focus 2 months later in a rib	Bloodgood
12 M 49	Vertebra (6th thoracic)	?		1 yr.	19 mos.*	4 yrs.		Laminectomy, 1300 mgm. hr. radium+X-ray therapy	G	Generalization occurred between 19 months and 4 years after observation of primary tumor	Peyton
13 F 38	Skull (parietal)	+	+	3 mos.	5 mos.*	3 yrs. 4 mos.		X-ray	G		Peyton
14 M 56	Femur (upper half)	o	+	1 mo.	2 yrs. 9 mos.*	About 3 yrs.		Curettage	G	Radiographic appearance of giant cell tumor	Bone Registry 710
15 M 57	Humerus (proximal half)	o	+	7 mos.	9 mos.*	2 yrs. 4 mos.		Resection, X-ray	G	Pathological fracture	Bone Registry 1597

*Time from first observation to generalization.
†G indicates generalization; S indicates a single lesion; N indicates that the case was proved by necropsy; R indicates that the other bones were examined roentgenologically.

TABLE OF CASES

Case Sex Age	Location of primary tumor	Bence-Jones protein		Time from onset of symptoms to 1st observation	Complete period of observation to time of case report	Time from primary tumor to death	Living	Treatment	Single or later generalized†	Remarks	Source of material
		Early stages	Later stages								
19 M 56	Vertebræ (4–8 thoracic)	0	0	6 mos.			8 mos. to date	Radiation treatment in progress. Laminectomy		Patient under therapy at present time. Questionable secondary focus left ilium	Michael Reese Hospital Tumor Clinic No. 2147
20 F 50	Femur (upper third)	?	?	2½ yrs.		6 yrs. 9 mos.		Biopsy		Radiographic appearance of giant cell tumor. Questionable secondary focus was present in lower dorsal vertebræ. This case is presented for differential diagnosis.	Bone Registry 1101

*Time from first observation to generalization.
†G indicates generalization; S indicates a single lesion; N indicates that the case was proved by necropsy; R indicates that the other bones were examined roentgenologically.

secondary lesion. The case is presented because of the striking similarity of the primary tumor to those in Cases 7, 9, 12, 18. At the present time the patient is receiving radiation therapy to the primary lesion.

CASE 20. American College of Surgeons Bone Registry. Case Number 1101.

This patient was a woman, age 50, who, about 2½ years prior to first examination, sustained a fracture of the hip. Function was regained but a tumor mass appeared at the site of fracture.

In July, 1926, the patient was operated on (Hospital for Joint Diseases, New York City). Microscopic examination of tumor tissue removed (Fig. 13) showed plasma cells. A diagnosis of plasma cell myeloma was made.

In August, 1926, the patient was admitted to the Memorial Hospital in New York City. X-ray examination (Dr. Herendeen) revealed a tumor causing bone destruction of the neck and greater trochanter of the right femur at the upper end of the shaft. The cortex was expanded and the trabeculated appearance suggested a giant cell tumor (Fig. 14).

X-ray examination of the chest in October, 1926, was negative. An X-ray film of the spine revealed evidence of bone involvement in the lower dorsal vertebræ.

In October, 1928, the patient's general condition was good.

In April, 1933, the patient died at her home. Cause of death is unknown.

A diagnosis of plasma cell myeloma was made from sections obtained at the first operation, and confirmed by the following pathologists of the Bone Registry of the American College of Surgeons: Drs. Morton, Ewing, Stewart, Copeland, Codman, Simmons, Hartwell, Coley, and Curphey. All emphasize the striking discrepancy between the radiological findings suggesting giant cell tumor and the histological findings of plasma cell myeloma.

This case presents a problem in diagnosis between the radiographic findings suggestive of giant cell tumor and the histological evidence of plasma cell myeloma. Bence-Jones protein is not reported. Thorough skeletal X-ray examination was made which revealed evidence of bone involvement in the lower dorsal vertebræ.

Although unable to classify this case as one of single plasma cell myeloma, we include it because of its diagnostic interest. It will be noted that other cases herein reported give radiographic evidence of giant cell tumor which, nevertheless, were proved histologically to be plasma cell myelomas.

RÉSUMÉ OF CASES

These cases of solitary myeloma may be separated into two groups; the first group comprising those cases in which the disease started as a single lesion and subsequently became generalized, and the second group comprising those cases in which the lesion remained solitary during the entire period of observation, either until death or until the time of the original report.

The first group (a solitary lesion later becoming generalized) is more important in support of the view that all so called multiple myelomas arise in a solitary focus and become generalized, and that only the rapidity of spread produces the clinical picture of multiple myelomas as it is usually seen.

The time interval between the definite diagnosis of a single myeloma and the later

proof of metastasis ranged from 2 months to 2 years 9 months (in the 5 reported cases: 2 months, 5 months, 9 months, 19 months, 2 years 9 months). In the case with the longest interval, the patient was treated by curettage of the primary lesion. This case will be discussed separately, inasmuch as the clinical and roentgenological signs are typical of a giant cell tumor.

In Case 12 we know only that the patient was still without metastases after 19 months and that the patient died with generalized metastases 4 years after the primary tumor had been discovered. This case was treated by laminectomy followed by interstitial radiation (1300 milligram hours) and external roentgen therapy.

The duration of life following the onset of generalization was: 1 month, 19 months, 29 months, 35 months. The primary focus in each case was: clavicle, vertebra, skull, femur, and humerus. In 2 of the cases of this group Bence-Jones protein was found in the urine at the time of the solitary lesion. In 2 cases it was found only after the condition had become generalized.

The second group (cases remaining solitary) contains 13 cases. Four of these patients were dead at the time of the original report. Two of them died 6 and 23 months after the first observation. Two died in surgical shock. Case 6, with a duration of life of 6 months, was treated by curettage of the femur. This case was diagnosed histologically (Askanazy) as myelosarcoma because of the malignant invading character of the growth. Five patients of this group were alive at the time of the original report, and by follow-up information it was determined that the duration of life since the first observation has been 12 months, 18 months, 1 year 7 months, 4 years, 10 years.

We call attention to the fact that 2 cases with long duration—considerably longer than the average course of this disease—received intense treatment. One of them (Case 4) was treated by curettage followed by interstitial radiation and subsequent amputation. At the time of the last examination (4 years after operation) the patient was alive and well, without signs of recurrence or generalization of the disease. The other case (Case 18) was originally treated by X-ray therapy followed by a stabilizing operation. One patient died only a few days after the original observation. We cannot draw any conclusions from this case, since the patient came under observation in a cachectic state with severe anemia, nephrosis, and thrombopenic purpura. In 3 cases of this group, we do not know the subsequent course of the disease.

In a recent editorial of the *Journal of the American Medical Association*, attention is called to a group of myelomas exhibiting solitary lesions. The benign nature of solitary lesions is emphasized. The cases reported in our communication seem to indicate that we can go one step further and recognize two groups of solitary myelomas. One group is solitary only in the beginning and subsequently becomes generalized. The prognosis in this group does not differ from that of multiple myeloma. The second, and rare group, may be called true solitary tumors. A prolonged observation (4 to 10 years) proves that they remain local.

The question arises as to whether all of the lesions which remained single belong to the same pathological entity. Cases of the first group show only that it has been possible to recognize a primary single lesion and observe its generalization. Some of the cases of the second group raise the question of whether the lesions remained single because the time of observation was not sufficiently long to observe a subsequent generalization. This objection may be applicable to Cases 1, 2, 6, 7, 8, 9, 10, and 17. In Cases 4, 5, and 18, with a duration of 4, 9, and 10 years, respectively, the time is long enough to assume that these cases will not become generalized. In seeking a reason for this we may ask whether the long duration is due to the treatment received. It is unlikely that the duration as a single lesion in Case 18 was due to the treatment, because the lesion did not respond to radiation. Whether or not Case 4, treated by curettage, radium puncture, and finally amputation, was cured by this treatment cannot be decided from this case alone.

It is of interest to note that the clinical and radiological appearance in Cases 4 and 18 was that of a giant cell tumor. In both of these

cases, however, the diagnosis of plasma cell myeloma was made by competent pathologists. On the other hand, we may note that this appearance of giant cell tumor in the radiological picture was shown not only in the 2 cases mentioned but also in 2 others (Cases 9 and 10). In 1 of these cases (Case 10) this radiological picture was accompanied by the histological findings of a malignant infiltrating growth differing from the typical picture of plasma cell myeloma. Furthermore, it may be noted that one of the single lesions which later became generalized (Case 14) likewise showed the clinical and radiological appearance of giant cell tumor and was curetted under this diagnosis.

Because of the interesting behavior of some of these tumors which show the clinical and radiological characteristic of giant cell tumor, and which nevertheless were proved histologically to be myeloma, we have included Case 20 in this report. An additional roentgenogram (Fig. 15) showing this discrepancy in radiological appearance in the same chest is presented. In the original findings of Case 20, with the radiographic appearance of giant cell tumor, the suspicion arose that a metastasis had already occurred. If this were true, this case would be very similar to Case 14 in its course. From these findings, there may be reason to believe that such cases have a different biological course from the typical plasma cell myelomas. However, the material herein presented is insufficient to do more than point out this possible variation.

SUMMARY

Eighteen cases of solitary myeloma of bone are reported; 12 cases from the literature, 5 from the Bone Registry of the American College of Surgeons, and 1 additional case. Two cases are presented as problems in radiological diagnosis.

In 5 cases the myeloma was solitary at the first observation and later became generalized. This is the behavior that is common to other types of malignant tumors. The only peculiarity of myeloma is the affinity for the osseous system which may be compared to the affinity of lymphosarcoma for the lymphatic system.

In 13 cases there was no generalization of the disease during the time of observation. In 7 cases the duration of the follow-up (longest duration 1 year and 7 months) is too short to permit the conclusion that these cases would not have become generalized. Two patients with observed myeloma 4 and 10 years were alive without generalization at the time of the report.

The location of the primary tumor was found in the clavicle in 1 case; in the maxilla in 1 case; in the humerus in 2 cases; in the skull in 2 cases; in the ilium in 2 cases; in the vertebræ in 4 cases; and in the femur (in all cases in the trochanteric region) in 7 cases.

In the cases of solitary myeloma which later became generalized, two had Bence-Jones proteinuria before generalization occurred. Two patients developed Bence-Jones proteinuria only after spread of the disease. Among the patients who retained a solitary myeloma throughout, 2 had Bence-Jones proteinuria. The finding of Bence-Jones proteinuria with a solitary lesion supports the diagnosis of myeloma, although this is not usually present in the early stage of the disease.

Certain of the cases show radiological and histological peculiarities. The radiological appearance in some of the cases was that of a giant cell tumor and in some a malignant invading growth was histologically noted. These peculiarities in the roentgenological findings and clinical course must be borne in mind in differentiating giant cell tumors and myelomas.

As to treatment, one cannot draw conclusions from the limited number of cases and the varied treatment used. It is well known that radiation therapy may control the disease over a certain period of time. We have no definite proof that intense treatment will cure the disease even though begun in the early stage before generalization has occurred.

We acknowledge with thanks the co-operation of Dr. Bowman C. Crowell for the use of material in the Bone Registry of the American College of Surgeons.

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STUDIES OF GALL-BLADDER FUNCTION

XIII. The Composition of the Gall-Bladder Bile and Calculi in Gall-Bladder Disease

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In 1863 Thudicum stated that biliary calculi resulted from a decomposition of the bile, the process being akin to putrefaction. Since that time we have been presented with the stasis-infection theory of Naunyn; the stasis-hypercholesteremia theory of Aschoff and Bacmeister; the physiochemical theory of Lichtwitz, and a host of others. The continued interest in the mechanism of biliary calculous formation is evidence that no one of the many theories already advanced satisfactorily explains the various types of calculi found in biliary tract disease.

The frequency of gall-stone disease has been well brought out by Mentzer (6) who reported an incidence of 15 per cent in the adult population of this country. Furthermore, biliary tract disease is the second most frequent indication for abdominal operations in general surgical practice.

We have previously reported (5) that when the gall bladder of man becomes damaged, there occurs a change in the composition of the gall-bladder bile. In this paper we are reporting data on the composition of the bile and calculi, when the latter were present, removed at operation from patients exhibiting various stages of gall-bladder disease. Although the composition of the gall-bladder bile at the time of operation may not be similar to the composition of the bile at the time calculi were being formed, the study of the bile in a variety of supposedly different pathological states and in the presence of calculi of dissimilar composition is of interest.

METHODS

The bile specimens were removed at operation by aspiration of the gall-bladder contents, the patients having had their last meal from 12 to 15 hours previous to operation. In the majority of instances the operation was done under spinal anesthesia.

The calculi found were imbedded in Wood's alloy. When the block became hard it was divided. One-half of the stone, imbedded in the alloy, was thus kept for permanent record and the other half was recovered by again melting the metal. This portion was powdered, dried in the oven at 105 degrees C. for 24 hours, and used for analysis. Analysis of the stone was made as follows: The dried powder was extracted in a Soxhlet with petroleum ether. The extract was evaporated to dryness and the cholesterol determined colorimetrically. The residue was extracted with 10 per cent hydrochloric acid. Calcium and phosphorus were determined in the neutralized extract by the methods of Clark and Collip and Youngburg and Youngburg, respectively. Pigment was extracted from the residue by boiling butyl alcohol and determined by the method of Hooper and Whipple with the modification of Rous and McMaster. The material left formed the "undetermined" residue.

The methods used for the chemical analyses of the bile have been reported by us in previous papers. No bile specimens were used which were contaminated with blood.

RESULTS

I. Non-calculous cholecystitis. In Table I are given the data from 26 patients with non-calculous cholecystitis. We realize that this group is not clearly defined and that although the clinical and laboratory examinations prior to operation may strongly indicate the presence of gall-bladder disease, the findings at the time of operation often do not confirm the pre-operative findings. Graham and Mackey have recently pointed out also that a diagnosis of chronic cholecystitis from histological sections is not always entirely reliable. In Table I we have, therefore, included only data from patients in whom the gross examination at opera-

TABLE I.—COMPOSITION OF BILE IN NON-CALCULOUS CHOLECYSTITIS

Patient	Calcium	Chloride	Bile salt	Cholesterol	Ratio	X-ray
	m.Eq. / L	m.Eq. / L	mgm. / 100 c.cm.	mgm. / 100 c.cm.		
No.	11	1	3180	1828	1.7	Visualized
Sc.		10	2000	409	4.9	Non-visualized
Ch.	6	12	3330	1248	2.6	Non-visualized
Sa.	24	17	4396			Visualized
Pe.	30	23	3740	122	30.6	Visualized
La.	23	26	4640	744	6.2	Non-visualized
He.	13	32	1650	148	11.1	Visualized
Ca.	22	37	9100	123	74.0	Non-visualized
Ar.	19	41	5963	176	33.8	Visualized
Su.	20	42	0	133		Visualized
Do.	15	42	3515			Visualized
Mo.	15	44	3230			Visualized
Hy.	18	54	1254	275	4.4	
Sc.	12	57	3000	303	9.9	
Ru.	12	58	4418			Visualized
Hu.	11	61	1090	78	14.0	
Bl.		69	2314			Visualized
McK.	36	71	4793	273	17.5	
Sa.	8	74	1600	294	5.4	Non-visualized
Ro.	10	82	1550	990	1.5	
Gr.	12	88	1390	132	10.5	Visualized
De.		95	4540			
Ma.	14	97	1926	242	7.9	Visualized
Gr.	10	106	0	40		Non-visualized
Mo.	4	116	30	4	6.8	Non-visualized
Fl.	8	118	500	104	4.8	

tion suggested cholecystic disease and which diagnosis the histological examination of the tissue later substantiated.

The calcium concentrations in this group varied from 4 to 36 milliequivalents per liter with a mean of 16 milliequivalents per liter. The chloride concentrations varied from 1 to 118 milliequivalents per liter, the mean being 57 milliequivalents per liter. The bile salt, expressed as sodium cholate, varied from 1 to 9,100 milligrams per cent with a mean of 2,813 milligrams per cent. The cholesterol concentrations were equally divergent ranging from 4 to 1,828 milligrams per cent with a mean of 383. In patient No. 8 the data on calcium, chloride, and bile salt show that the gall bladder was concentrating practically normally although the gall bladder failed to be visualized on several occasions after the administration of sodium tetraiodophenolphthalein; while in patient No. 6 the gall bladder was visualized even though the evidences of bile concentration, at least as regards calcium and bile salt, were not nearly so good.

Of the 26 specimens 19 had a chloride concentration below 80 milliequivalents per liter, while in 4 instances the concentration was below 20 milliequivalents per liter, which we believe to be within the normal range. In not a single instance in the entire group, however, were the chloride, calcium, and bile salt concentrations all within the normal range for gall-bladder bile. The general tendency was for the lower calcium concentrations to be associated with the higher chloride and lower bile salt concentrations. There were, however, many exceptions to this general rule.

II. Calculous cholecystitis—In Tables II and III are given the data from the specimens obtained from the chronically diseased gall bladders containing calculi. They are divided into two groups depending upon the ability of the gall bladder to be visualized after the administration of sodium tetraiodophenolphthalein. In Table IV are given the data obtained from the bile in gall bladders containing stones but in which there was evidence at operation of an acute cholecystitis.

In Group A (chronic calculous cholecystitis—gall bladder visualized), the calcium values varied from 5 to 44 milliequivalents per liter with a mean of 15. The chloride concentrations ranged from 7 to 110 milliequivalents per liter the mean being 61; while the bile salt concentrations varied from 0 to 7,350 milligrams per cent, with a mean of 1,560. The cholesterol concentrations ranged from 0 to 1,600 milligrams per cent, the mean being 480.

When the gall bladder had not been visualized by the X-ray after dye administration (Group B), the calcium concentrations were found to vary from 2 to 25 milliequivalents per liter with a mean of 10, and the chloride concentrations varied from 57 to 140 milliequivalents per liter with a mean of 102. In this group the bile salt concentration ranged

TABLE II.—THE COMPOSITION OF BILE AND STONES IN CALCULOUS CHOLECYSTITIS GALL BLADDER VISUALIZED

Patient	Bile					Stone							
	Calcium	Chloride	Bile salt	Cholesterol	Ratio	H_2O	Calcium	PO_4	Pigment	Cholesterol	Residue	Recovery	
	m.Eq./L	m.Eq./L	mgm. per cent	mgm. per cent		Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	
He.	10	7	1000	78	12.8	2.1	0	0	Trace	96.4	4.2	102.7	Whole stone
Li.	15	21	7350	—	—	4.9	1.0	0.3	0.2	86.6	3.2	96.2	Center
						0.4	2.8	Trace	0.4	96.8	4.6	105.0	Periphery
Ri.	23	34	2370	344	6.8	11.1	22.1	1.2	3.7	0.5	21.0	59.6	Whole stone
Br.	27	38	1230	759	16.0	¤	1.0	Trace	2.7	96.0	0.3	100.0	No. 2
						4.5	4.9	Trace	0.6	79.6	¤	92.2	No. 1 center
						3.2	2.6	0.3	4.5	87.1	5.9	103.6	No. 1 periphery
Po.	12	40	1000	252	3.5	0.9	14.5	2.1	1.7	41.0	10.1	70.3	Center
						0.9	14.0	0.2	1.0	59.6	7.8	83.5	Periphery
Va.	—	41	2840	997	2.8	1.5	2.6	0	0.7	78.3	6.5	89.6	No. 1
						4.6	0	0	1.5	73.9	0.6	80.6	No. 2 center
						3.0	9.9	0.6	2.0	65.1	1.3	82.5	No. 2 periphery
So.	—	48	800	—	—	4.4	¤	¤	Trace	92.7	3.6	100.7	Whole stone
Lit.	13	53	83	787	0.1	10.1	3.7	0.3	0.1	80.0	—	94.2	Whole stone
Do.	8	55	1900	1600	1.1	1.1	4.8	0.2	2.0	87.6	0.4	96.1	Whole stone
Pof.	24	59	1200	320	3.7	0.5	2.1	Trace	0.6	116.0	2.1	121.3	No. 1
						0.4	6.3	Trace	0.4	96.0	0	103.1	No. 2
Br.	14	59	1330	278	4.7	3.4	3.9	0	Trace	87.3	9.2	103.8	Whole stone
Tr.	—	59	Trace	—	—	22.6	¤	0	Trace	67.0	¤	89.5	Whole stone
Fo.	11	60	1875	377	5.0	1.1	1.8	Trace	Trace	104.8	0	107.7	Whole stone
Sm.	23	61	3600	400	9.0	0.2	1.6	0.1	0.5	79.6	¤	82.0	Whole stone
Os.	14	62	3120	368	8.5	1.1	Trace	¤	Trace	88.0	¤	89.1	Whole stone
It.	8	64	1800	1140	1.5	4.1	0	0	0.5	99.9	Trace	104.0	Whole stone
Ro.	6	67	950	97	9.8	2.0	15.7	0	27.2	25.7	—	70.6	Whole stone
Re.	12	67	0	209	—	4.3	7.3	Trace	0.2	76.9	—	88.7	Whole stone
We.	10	68	2880	445	5.1	4.0	12.5	0.3	0.9	74.5	4.9	97.1	Whole stone
Si.	6	69	1880	195	9.6	4.3	3.6	Trace	0.8	77.6	0	86.1	Center
						4.3	3.4	Trace	Trace	81.2	¤	88.6	Periphery
Ha.	8	81	830	—	—	0.5	12.0	Trace	1.5	30.3	12.5	56.6	Whole stone
Ba.	12	83	0	339	—	0.9	11.0	0	1.1	79.3	12.8	105.1	Whole stone
Wa.	—	90	980	765	1.2	3.9	0	0.4	0.5	88.8	8.3	101.9	Center
						3.8	0	0.1	0.4	109.0	0	113.3	Periphery
Ca.	5	93	0	0	—	3.8	28.5	Trace	3.9	58.0	7.9	100.9	Center
						3.1	26.0	0.3	3.8	62.3	7.8	103.3	Periphery
Kr.	44	106	—	—	—	8.3	Trace	Trace	0.4	85.0	6.2	99.9	No. 1 center
						4.8	5.3	1.3	1.0	70.8	12.1	95.3	Periphery
						4.1	Trace	0	0.3	80.3	27.1	111.8	No. 2 center
						0.8	0.8	Trace	0.8	97.0	—	99.4	Periphery
Ma.	16	110	0	—	—	0.3	¤	0	Trace	82.6	0.9	83.8	No 1
						3.1	1.9	0	0.1	71.3	24.8	101.2	No. 2
Gr.	—	—	—	—	—	4.6	Trace	0.1	0.2	98.0	0	102.8	Whole stone
Wi.	—	—	—	—	—	4.5	Trace	Trace	Trace	97.9	0	102.5	Whole stone
Mi.	—	—	—	—	—	4.7	¤	Trace	0.5	91.5	0	96.6	Center
						4.0	1.2	Trace	Trace	82.7	0	87.9	Periphery

TABLE III.—THE COMPOSITION OF BILE AND STONES IN CALCULOUS CHOLECYSTITIS GALL BLADDER NOT VISUALIZED

Patient	Bile					Stone							
	Calcium	Chloride	Bile salt	Cholesterol	Ratio	H_2O	Calcium	PO_4	Pigment	Cholesterol	Residue	Recovery	
	m.Eq./L	m.Eq./L	mgm. per cent	mgm. per cent		Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	
Ka.	—	57	3080	312	9.6	2.0	3.1	0.7	3.1	19.8	61.4	90.1	Whole stone
Al.	14	63	1250	121	10.3	7.2	2.4	0	Trace	84.0	0	93.6	No. 1
						0.1	1.0	Trace	0.1	101.0	Trace	102.2	No. 2
Ba.	14	75	80	114	0.7	15.8	1.9	Trace	Trace	80.3	—	98.0	Whole stone
Fo.	8	77	1460	356	4.1	6.3	1.9	0	1.2	87.5	8.6	105.5	No. 1
						8.4	6.6	0	0.7	74.3	9.1	99.1	No. 2 center
						5.4	1.3	0	0.3	70.0	3.6	80.6	Periphery
Ga.	7	93	0	59	—	0.5	2.2	Trace	0.2	83.0	1.1	87.0	Center
						1.9	12.1	Trace	1.9	40.0	19.3	65.2	Periphery
Mi.	6	94	708	242	2.9	6.0	1.7	0.3	0.4	79.4	1.9	89.7	No. 1
						4.0	2.5	0	0.3	77.5	4.8	89.1	No. 2 center
						0.4	1.1	Trace	0.3	101.0	0	102.8	Periphery
Sc.	13	101	0	98	—	2.5	3.6	1.0	0.2	48.0	0.6	55.9	Center
						2.0	5.9	8.9	1.4	72.0	0.4	90.6	Periphery
Sm.	10	101	3140	154	20.4	12.0	5.6	1.2	8.9	3.4	—	31.1	Center
						2.2	6.1	2.5	28.8	1.2	29.6	—	Periphery
Fa.	—	102	0	—	—	3.7	Trace	Trace	Trace	92.8	0	96.5	Whole stone
Ja.	6	108	0	1	—	5.0	2.2	Trace	0.7	83.1	0	91.0	Whole stone
Bo.	2	110	0	—	—	0.7	2.6	0	0.2	89.5	0	93.0	Center
						1.7	2.9	Trace	2.2	70.6	23.7	100.2	Periphery
Sc.	11	112	0	52	—	0.2	0	0	0.7	101.3	2.0	103.5	Center
						2.3	0	0	0	99.0	1.0	102.3	Periphery
Go.	4	120	610	272	—	4.7	0	Trace	0.4	99.0	0	104.1	Center
						4.3	3.3	Trace	10.7		12.6	64.9	Periphery
Ho.	—	120	Trace	—	—	3.6	6.3	2.7	Trace	76.8	0	89.5	Center
						3.5	5.4	1.2	0.3	59.3	5.1	74.9	Periphery
Le.	16	134	Trace	27	—	4.8	0	0	0.5	75.1	3.6	83.9	Whole stone
Wa.	6	135	0	28	—	4.2	0	0	0	98.2	1.0	103.4	No. 1 center
						3.9	0	Trace	0.2	89.9	12.3	106.4	Periphery
						9.0	0	Trace	0.2	85.8	0	95.3	No. 2
Ch.	25	140	0	26	—	0.4	11.8	0.5	0.5	45.1	10.9	59.2	Whole stone
Gr.						1.1	6.7	0.3	1.8	63.0	0.7	73.6	Whole stone
Go.						17.3	8.1	Trace	7.0	50.9	—	83.3	Center
						9.1	2.2	Trace	1.0	64.0	—	76.3	Middle
						5.0	1.2	0	0.3	57.3	—	78.5	Periphery
Gu.						4.0	0	Trace	1.8	50.0	0	55.6	Common duct
						4.2	0	0.3	0.9	91.0	7.0	102.3	Gall bladder
Ro.						4.7	Trace	Trace	Trace	97.9	0	102.5	Whole stone
Pe.						4.4	3.9	Trace	Trace	84.6	0.4	93.2	Whole stone
St.						4.0	0	0.1	0.6	94.0	2.9	101.7	Center
						2.8	0	Trace	1.7	88.8	0	93.3	Periphery

TABLE IV.—THE COMPOSITION OF BILE AND STONES IN ACUTE CALCULOUS CHOLECYSTITIS

Patient	Bile					Stone							
	Calcium	Chloride	Bile salt	Cholesterol	Ratio	H_2O	Calcium	PO_4	Pigment	Cholesterol	Residue	Recovery	
	m.Eq./L	m.Eq./L	mgm. per cent	mgm. per cent		Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	
Si.		45	1030	625	—	9.6	1.4	Trace	1.8	69.8	0.3	82.9	Whole stone
Sp.	12	68	—	—	—	0	23.4	1.9	0	32.4	—	57.7	Center
						0.4	6.1	2.9	0.3	75.7	3.4	88.8	Middle
						1.7	11.1	1.4	0.2	60.9	33.7	109.0	Periphery
Ca.	9	72	4100	—	—	1.0	9.0	0	0.7	72.7	3.0	86.4	Whole stone
La.	7	83	0	115	—	4.7	5.8	Trace	1.1	89.2	—	99.8	Whole stone
Da.	8	86	0	277	—	4.3	2.3	Trace	1.2	82.3	—	90.1	Whole stone
Go.	7	91	658	88	7.0	1.7	4.0	2.0	1.0	76.1	2.0	86.8	Whole stone
Br.	7	94	0	108	—	3.6	0	Trace	0.2	98.8	0	102.6	Whole stone
We.	7	94	Trace	533	—	4.0	0	0	Trace	80.7	1.8	86.5	Whole stone
Ho.	4	95	83	55	1.5	3.7	3.5	0	0	85.9	—	93.1	Whole stone
Wei.	6	100	0	—	—	4.0	Trace	0.4	0	97.8	0.9	102.8	Whole stone
Ar.	10	102	930	136	6.8	0.6	0.9	Trace	0	97.0	0	98.6	Whole stone
Gr.	7	105	1080	163	6.6	3.4	0	1.1	3.4	84.0	2.4	94.2	Center
						2.2	19.2	Trace	0.3	42.5	4.3	68.6	Periphery
Ka.	4	113	420	163	2.0	4.0	3.2	Trace	1.5	68.5	2.9	80.1	Whole stone
Ma.	5	119	0	8	—	5.3	12.7	Trace	1.0	65.0	10.6	94.6	Center
						1.6	3.8	Trace	1.3	61.0	10.6	78.3	Periphery
Sh.	3	126	370	122	2.0	5.0	2.9	Trace	1.5	68.5	2.9	80.1	Whole stone
Wi.	3	132	0	3	—	0.3	1.2	Trace	1.0	105.0	0.6	—	Whole stone
Ha.	7	133	0	27	—	2.6	0	0	0.6	83.1	4.5	90.8	Center
						6.5	0.5	0	0.1	84.7	0	91.7	Periphery
Sa.	5	136	31	81	0.4	2.9	8.6	2.1	28.0	8.3	50.6	100.5	Whole stone
Br.	6	141	0	Trace	—	4.1	7.5	0.1	0.9	76.7	0	81.8	Whole stone
Gu.	—	—	—	—	—	1.1	0	Trace	Trace	69.7	0	70.3	Whole stone
Sp.	—	—	—	—	—	6.0	2.3	0	0.3	70.6	0.8	80.0	No. 1 center
						8.9	2.8	0	0.6	78.0	1.3	91.6	Periphery
						5.6	0	0	0.4	77.2	1.8	85.0	No. 2 center
						5.4	0	0	0.4	79.8	4.5	90.1	Periphery

from 0 to 3,140 milligrams per cent with a mean of 607, while the cholesterol concentrations varied from 1 to 356 milligrams per cent with a mean of 133.

In the acute cases (Table IV) the calcium concentrations varied from 3 to 12 milliequivalents per liter, the mean being 6.5, while the chloride content varied from 45 to 141 milliequivalents per liter with a mean of 101. The bile salt concentration varied from 0 to 4,100 milligrams per cent with a mean of 483; while the cholesterol concentrations were found to vary from 0 to 625 milligrams per cent with a mean of 150.

The data in this latter group are without doubt influenced in part by the acute infection present at the time of operation. In general, they are not unlike the data obtained from the non-visualized chronic stone cases. The mean bile salt value is lower and the mean cholesterol concentration is slightly higher, although the cholesterol concentrations are not as high as one might expect to find in the presence of acute infection.

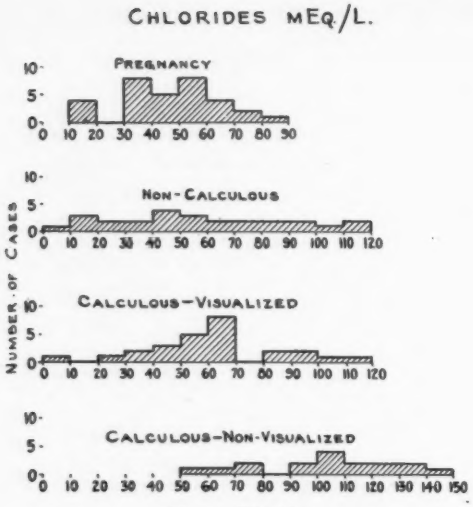

Fig. 1. Chlorides.

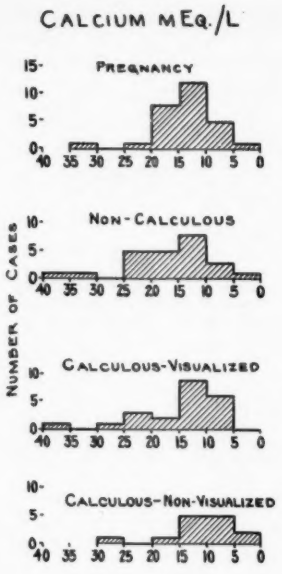

Fig. 2. Calcium.

Stones from 73 different gall bladders were subjected to analyses. Roentgen examination of the gall bladder was available in 52, while in 21 instances the patient was not subjected to roentgen studies. The analytical data are given in Tables II, III, IV. It can readily be seen that the major portion of each of the stones which we studied consisted of cholesterol. In only a few instances did the calcium content reach 20 per cent of the weight. The recoveries in the majority of instances so closely approximate 100 per cent that the amount of undetermined substances present in the calculi was as a rule very small.

One might expect that chemical analysis of the stones would show that the stones which were visualized as opaque shadows would be those with a high calcium content. This was not found to be the case. Of the stones visualized as opaque shadows, 19 had a calcium content of less than 10 per cent, the remainder having a content of between 10 and 25 per cent. In the entire group of 73 stones from different patients, 61 had a calcium content of less than 10 per cent. It is clear, therefore, that in the group studied the calcium content of the stones was small.

In contrast to the calcium content, the cholesterol content of the stones was high, 67 having a content of more than 40 per cent. Of the 25 stones which were visualized as opaque shadows, after cholecystography, 21 had a cholesterol content of over 40 per cent. No pure pigment stones were encountered in this series. In 2 instances where it appeared that the calculus might consist chiefly of bile pigments, chemical analysis demonstrated a considerable amount of cholesterol and organic débris and only a small amount of bile pigment.

From this series, it would appear safe to state that positive visualization of the stone after cholecystography gives no indication of its chemical composition. None of the calculi could be considered primary calcium stones, the majority being cholesterol stones with varying amounts of calcium, pigment, and organic débris.

From our data there would appear to be no correlation between the composition of the gall-bladder bile found at operation and the type of stone found in the gall bladder. Biles of highly similar composition were found in gall bladders containing practically pure cholesterol stones and in gall bladders containing mixed stones.

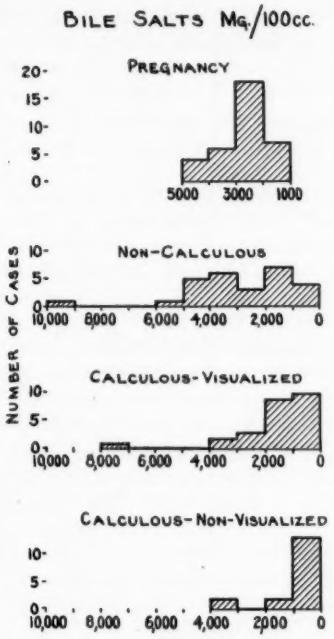

Fig. 3. Bile salts.

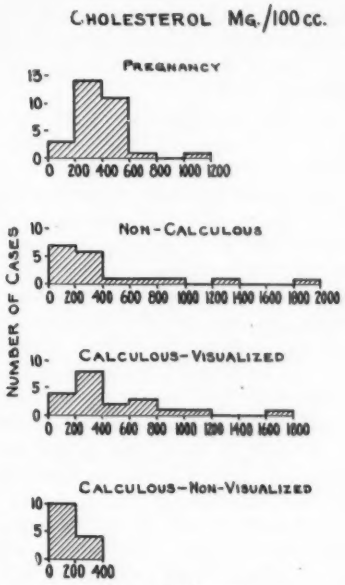

Fig. 4. Cholesterol.

EVALUATION OF STUDY

It is now generally agreed that the normal gall bladder changes the composition of the hepatic bile in a consistent manner. With the absorption of water from the bile the gall bladder removes chloride and bicarbonate so that the concentrations of these substances in normal gall-bladder bile is only a fraction of their concentrations in the hepatic bile (5, 8). Calcium, bile pigment, bile salt, and cholesterol are concentrated in the gall bladder (4, 9, 10). The evidence at present strongly suggests that normally small amounts of calcium and bile salt are absorbed from the bile while concentration is taking place, and that bile pigment and cholesterol remain quantitatively in the gall bladder during the process of concentration.

The data presented in this paper demonstrate that in the presence of cholecystitis the absorbing function of the gall bladder becomes altered.

As the gall-bladder wall becomes damaged the chloride concentration of the gall-bladder bile rises. This increase in the chloride concentration of the gall-bladder bile may be due to failure of the gall bladder to remove the chloride coming to it in the hepatic bile, or to chloride coming into the bile with any fluid passing into the gall bladder from its wall, or to a combination of these factors.

The decrease of the calcium concentration in the specimens from damaged gall bladders may also be the result of several factors. The low concentrations frequently encountered in the specimens of gall-bladder bile which we examined may be due to failure of the gall bladder to concentrate the hepatic bile or to the removal of calcium from the solution. Evidence which we have previously reported indicated that under the condition of a high carbon dioxide in the gall-bladder bile the calcium in the gall-bladder bile would be partly precipitated as calcium carbonate. It is also possible that under the condition of a damaged wall the gall bladder is more permeable to the passage of the calcium ions than normally.

The most constant indication of a disturbance of function is a decrease in the bile salt

concentration. With increasing evidence of a disturbance of gall-bladder function, there is nearly uniformly a parallel decrease in the bile salt concentration.

It was not possible, however, to find a parallelism between the conventional pathological diagnosis and the changes in the chemical composition in the gall-bladder bile. In certain instances the bile was removed at a time when the lesion of the gall-bladder wall was progressively becoming more abnormal. In other instances the inflammation which previously had seriously impaired the concentrating function of the gall bladder was subsiding, at least to the extent that some concentration of the bile was being accomplished.

No consistent differences were found between the composition of bile in gall bladders containing cholesterol stones and the bile from gall bladders containing stones of the mixed type. There was also no constant direct relationship between pathological classification of the gall bladder and chemical composition of the bile, although it is possible to demonstrate certain gross differences between the biles of the various pathological groups.

Figures 1, 2, 3, and 4 show the distribution of chloride, calcium bile salts and cholesterol in (a) gall-bladder bile from pregnant women at term, in (b) non-calculous cholecystitis and in (c) and (d) chronic cholecystitis with calculi, the latter group being divided into those gall bladders which were, and were not visualized roentgenographically after the administration of sodium tetraiodophenolphthalein.

It can be seen that as the clinical evidence of increased impairment of function was found the frequency of the chloride concentrations in the higher brackets increased. In a similar manner the frequency of very low concentration of calcium and bile salts increased.

The bile salt concentrations in the pregnancy group were higher than in any of the other groups except for an occasional specimen. In the non-visualized calculous group, the greatest number of specimens contained less than 1,000 milligrams per cent of bile salt.

The cholesterol concentrations varied considerably but they were consistently higher in the pregnancy group and lower in the calculous non-visualized group in which a low bile salt concentration was found. In the pregnancy group, the bile salt concentration was apparently sufficient to keep a high concentration of cholesterol in solution in bile.

These data indicate certain trends in the chemical composition. We do not feel that they should at this time be treated on a statistical basis, even though when so treated some of the differences between groups appear significant. They nevertheless indicate that in the various stages of cholecystitis, as they are now conventionally given, the degree of impairment of the normal mechanism of concentration varies widely. The mere presence of calculi does not always in itself indicate that this mechanism is more pathological than may be encountered in a gall bladder which does not contain stones but which is the site of an inflammatory change.

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UNRECOGNIZED POSTOPERATIVE INFECTION

A Cause of the Syndrome of So Called "Liver Shock"[1]

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NUMEROUS articles dealing with the causes of death following operations upon the gall bladder and the biliary tract are to be found in the surgical literature of the past decade. A review of these articles discloses that the reason for individual fatality, in most instances, was recognized readily. In not a few cases, however, the cause of death remained obscure. Such unexplained deaths, when preceded by a postoperative clinical course which will be described presently, were attributed most commonly to a condition which has been termed "liver shock" ("liver death," "rapid high temperature death"). A recent increase in the number of articles devoted specifically to this topic or making reference to it, indicates renewed interest in the subject on the part of physician and surgeon alike. Among those who have made contributions may be mentioned:—Heyd (13, 14, 15), Cave, Behrend, Stanton, Connell (5, 6), Doran and co-workers, Eiss, Shearer, Weiss, Cutler, Schutz, Helwig and Kuhn (20), Guthrie and Robertson, Sharples, Sutton, Boyce (2, 3), and McFetridge (3).

Heyd, who apparently first called attention to "liver shock" following surgical procedures upon the gall bladder and the biliary tract, divides such cases into three groups. The latter may be described briefly as follows:

Type I. In this group are included only cases which are subjected to simple cholecystectomy. The patients are neither jaundiced nor acutely ill at the time of operation. Shortly after operation there develops without apparent cause, rapidly rising temperature, delirium, and vasomotor collapse. This is followed by coma and death, the latter as a rule occurring within 24 to 48 hours.

Type II. These patients have had a previous cholecystectomy and occasionally a drainage of the common duct. Operation is performed for the relief of obstructive jaundice. Convalescence is satisfactory for the first few days. Then the biliary drainage diminishes in amount, and becomes progressively more watery in character. In spite of diminishing jaundice, the patient becomes delirious, then stuporous, and finally comatose. Exitus occurs in a state resembling cholemia, as noted in patients with unrelieved obstructive jaundice.

Type III. These patients are not jaundiced. They usually are suffering from disease of the common duct or pancreatitis, for which choledochotomy with drainage is performed. For the first 24 to 36 hours, convalescence is satisfactory. Then the pulse rate becomes accelerated and the patient presents the picture of shock associated with vasomotor collapse, followed by oliguria, then anuria, uremia, fever, and finally coma ending in death.

As Cutler has pointed out, Types II and III seem to be in some measure predictable, or at least susceptible of explanation on the basis of prolonged jaundice with probable liver damage on the one hand, and upon diminished renal function on the other. Type I however, in view of the excellent general condition of the patient prior to operation, occurs entirely unexpectedly and appears to be entirely unpredictable. It is with this type alone, that we are concerned in this communication. Accordingly, the term "liver shock," as employed by the author, henceforth shall designate Type I only, unless specified otherwise.

The syndrome occurring in Type I "liver shock," as described by several authors (4, 5, 6, 7, 8, 14, 15, 22), may be presented in more detail as follows: Within several hours of cholecystectomy, the temperature commences to rise without apparent cause. The rise is progressive, and is accompanied by a corresponding increase in pulse and respiratory rates. Within 12 to 24 hours, temperature reaches 104 to 107 degrees, and the pulse

[1] From the Surgical Service of Dr. Harold Neuhof, The Mount Sinai Hospital, New York City. Delivered before the Surgical Section of the New York Academy of Medicine, January 3, 1936.

becomes extremely rapid, soft, and often thready. The skin becomes cold and clammy, blood pressure falls, and cerebral excitation frequently occurs. As the temperature continues to rise, the patient becomes stuporous and finally comatose, the terminal state being one of shock and vasomotor collapse, associated with hyperpyrexia. Death as a rule occurs within 24 to 48 hours following operation, but occasionally may be further delayed by vigorous therapy. It has been stated that the more common fatal postoperative complications, such as peritonitis, hemorrhage, pneumonia, embolism, etc., can be ruled out readily on clinical grounds. Under such circumstances, because of the lack of evidence of any obvious lesion to account for the patient's unusual course following operation, the diagnosis of "liver shock" is commonly made. According to Boyce and McFetridge (3), the only significant finding to be noted at postmortem examination is degeneration (microscopic) of the liver of varying degree. Connell (6), on the other hand, stated that he had repeatedly failed to find sufficient liver abnormality at postmortem examination to explain death. Whether hepatic degeneration, when it exists, is the cause of death or is merely the evidence of some profound intoxication is still the subject of debate. Considerable difference of opinion has been expressed also as to the mechanism involved in the production of the syndrome under discussion. Some of the theories which have been evolved are based purely on clinical observation, others on the results of postmortem examination, and still others on animal experimentation. Since they are not germane to the subject of our discussion they will not be reviewed, but those who are interested will find ample material for consideration in the articles listed in the appended bibliography.

In connection with our discussion, it is significant that in the literature the reported incidence of "liver shock" following cholecystectomy varies widely; the range being from 0 to 34 per cent. Such variation in incidence reported by observers who employed a fairly well standardized technique in operating upon a clearly defined group of patients, led us to examine the criteria which were employed in establishing the diagnosis. It was found almost at once that these criteria were far from uniform and that they varied not only with different authors but also with individual cases in series reported by individual authors. Thus, in certain cases, the diagnosis was based entirely on clinical and laboratory data. In others, the clinical diagnosis appeared to be confirmed by incomplete postmortem examination; while in still others, it appeared to be confirmed by complete postmortem examination. *In the great majority of instances, no postmortem examinations of any type were performed. In the comparatively small number of cases in which autopsies were performed, few appeared to be adequate.* The author designates as "adequate," only those examinations which included a study of the brain and spinal cord whenever the routine examination of the abdominal and thoracic contents proved negative.

It is realized that often it is difficult to obtain permission to perform postmortem examination. Nevertheless, lacking such examination, the question arises as to whether it is justifiable to accept a diagnosis of "liver shock" without reservation. It is to be emphasized that this diagnosis is one of exclusion, and is permissible only after all other complications responsible for hyperpyrexia and early death have been ruled out. It may be claimed that such "ruling-out" is not difficult, and that postmortem confirmation, although desirable, is not essential. By way of answer, one has only to recall the desperate condition of the patient following operation, the extremely toxic state, the restlessness due to delirium, or the lack of co-operation resulting from stupor, to realize that the accurate elicitation of physical signs and symptoms of some of the more common postoperative complications often is difficult or impossible. The author now proposes to demonstrate the correctness of this statement. In the first place, it will be shown that virulent infection may produce a clinical syndrome which is identical with that of so called "liver shock." Secondly, it will be demonstrated that the evidence of such infection may not be detected because the patient may

be so acutely ill as to be incapable either of being examined thoroughly or of co-operating with the examiner in the elicitation of existing physical signs. Finally, it will be shown by postmortem studies that patients in whom the clinical diagnosis of "liver shock" was entertained or actually made for apparently justifiable reasons died of other complications.

As has been stated previously, it is not our purpose to discuss the various causes of "liver shock," nor to question whether or not such an entity exists. It is our object, rather, to point out various pitfalls that are to be avoided in making the diagnosis and to emphasize the fact that serious errors may be committed if care is not exercised to corroborate the clinical diagnosis by adequate postmortem examination. The implication, under such circumstances, is that many unconfirmed clinical diagnoses are incorrect and that therefore the incidence of genuine "liver shock" must be considerably less than has been stated by some; unless one includes under the diagnosis of "liver shock," all cases of high temperature and early death after cholecystectomy, the causes of which are not determined.

The author became interested in the subject as the result of an experience (Case 1) in which a death which appeared unquestionably to be due to "liver shock," was found at subsequent postmortem examination to have been caused by unrecognized extensive subphrenic suppuration. Not only was the latter not detected during life, but its presence was not even suspected. In this connection, the following quotation from Stanton is significant: "Subdiaphragmatic abscess is very rarely diagnosed clinically. On the other hand, it appears to be rather frequently found at autopsy. I believe that it is a more frequent complication of gall-bladder operations than the figures would indicate."

As a result of the experience cited, the surgical records of the Mount Sinai Hospital for the years 1928 through 1933 were investigated, for the purpose of subjecting suspected cases of postcholecystectomy "liver shock" to more intensive study. During the above period 1,360 cholecystectomies were performed, of which only those that terminated fatally were reviewed. Of the fatal cases, a study was made *only of those in which the postoperative course was unexplained on clinical grounds and at the same time corresponded with that of so called "liver shock."* Of these, *we excluded all cases that were not subjected to complete postmortem examination or to examination that was sufficiently complete to explain readily, the cause of death.* All patients who were jaundiced or acutely ill at the time of operation were eliminated from consideration, as were those who had been subjected to previous operative procedures on the gall bladder and the biliary tract.

The material consists therefore of a series of cases, subjected to simple cholecystectomy with drainage, in which the patients were neither jaundiced nor acutely ill at the time of operation and had not been subjected to other operations upon the gall bladder or the biliary tract. Following operation they developed without apparent cause, the classical syndrome of rapidly rising temperature and shock, with early fatal termination; and were subjected subsequently to adequate postmortem study. It will be seen that these cases, of which there were 4, correspond to those which Heyd has designated as "liver shock," Type I.

CASE REPORTS

CASE 1. M.F., a female, 26 years old, was admitted to The Mount Sinai Hospital with a history of recurrent, typical attacks of acute cholecystitis. The present attack began 3 days before admission and was characterized at onset by sudden, severe, cramp-like pain in the right upper quadrant, which radiated to the back. Pain was accompanied by fever and vomiting. At the time of admission, the former had begun to subside.

On physical examination, temperature was 102 degrees; pulse, 100; and respiration, 20. White blood cells numbered 13,300. Polymorphonuclear leucocytes were 88 per cent. A tender mass was present in the right upper quadrant, but muscular rigidity was absent.

The patient was observed for 7 days. during which the temperature and pulse rate gradually fell to 99 and 66 degrees, respectively. Spontaneous pain disappeared, although slight tenderness and a palpable mass remained. X-ray examination, after the oral administration of dye, revealed faint visualization of the gall bladder but no stones.

On the afternoon of the eighth day following admission, operation was performed under nitrous oxide gas oxygen ether anesthesia. A distended gall bladder, filled with turbid grayish fluid and containing a single mulberry stone impacted in the ampulla, was found. Cholecystectomy with drainage and incidental appendicectomy, were performed. Operation was uneventful and the patient was returned to the ward in good condition. During the night her temperature gradually rose, and by morning (16 hours after operation) had reached 104.8 degrees. At that time, pulse was 148 and respirations 36. The abdomen was soft, not tender, and not distended. Six hours later (22 hours after operation) temperature was 108.4 degrees, pulse was 180, blood pressure was 60/0, and the patient was comatose and in profound shock. In the meantime, vigorous and continuous antishock therapy had been instituted. Although the temperature could be brought down by means of ice-packs, ice-cold colonic irrigations, and anti-pyretics administered intravenously, it would again rise quickly to its former level. After lapsing into coma 24 hours after operation, the patient never regained consciousness, although life was sustained for 48 hours by means of continuous, day and night therapy.

Repeated hemoglobin readings of 98 per cent seemed to preclude hemorrhage as the cause of the clinical picture. Diffuse peritonitis was ruled out on clinical grounds, as well as by two negative peritoneal aspirations. The day before death, the blood urea-nitrogen was 35 milligrams per cent. Urinary output remained adequate at all times. The clinical picture of unexplained rapidly-rising fever, rapid pulse and respiratory rates, profound shock, coma, and death in hyperpyrexia, made the diagnosis of "liver shock" appear practically certain. The diagnosis seemed further supported by the absence of evidence of intra-abdominal hemorrhage, peritonitis, or pneumonia. The increased blood urea nitrogen, as pointed out by Heyd, appeared to confirm further, the diagnosis.

At postmortem examination the essential findings, much to our surprise, were as follows:

1. Large serofibrinopurulent subphrenic abscess (right side).
2. Acute serofibrinous pleuritis (supradiaphragmatic) (right side).
3. Acute serofibrinous peritonitis (localized to the operative site). Culture of pus from subphrenic abscess: Streptococcus hemolyticus and Staphylococcus aureus.

If postmortem examination had not been performed in this case, it would have been justifiable on clinical grounds, to attribute death to "liver shock." Autopsy, however, demonstrated that virulent intraperitoneal infection was responsible for the lethal outcome. It is important to note that the clinical manifestations of infection were so fulminating that their significance was not appreciated during life.

CASE 2. R.N., a female, 40 years of age, was admitted to The Mount Sinai Hospital for the correction of a complete prolapse of the uterus. She also gave a history of occasional attacks of right sided abdominal pain, in the upper and lower quadrants, which radiated to the right shoulder blade. There had never been any other associated symptoms. The last attack had occurred 6 weeks previously.

On admission, the temperature and pulse rate were normal. A moderately tender, globular mass was palpated in the right upper quadrant. X-ray examination after the oral administration of dye, performed on the day following admission, revealed a ring shadow 1 inch in diameter in the region of the gall bladder.

The temperature and pulse rate remained normal during an 8 day period of observation, but mild, right upper quadrant pain persisted. Because of the latter, it was decided to proceed with cholecystectomy and to postpone operation for the uterine prolapse until a later date.

On the ninth day after admission, cholecystectomy with drainage and incidental appendicectomy were performed. The gall bladder was hydropic and contained a single large stone which was impacted in the region of the ampulla. The operative procedure was easily performed, the viscus being removed from below upward.

Following operation, there was a steady rise in temperature and pulse rate. At the end of 36 hours, temperature was 106.2 degrees, respiratory rate was 40, pulse was almost imperceptible, and the patient was semi-comatose and in shock. The abdomen was soft, non-tender, and not distended. There was a free discharge of bile stained fluid along the drain. There was no clinical evidence of intraperitoneal or extraperitoneal hemorrhage. The characteristic clinical picture of "liver shock" was present, and the diagnosis appeared self-evident. At that time, the following significant note was made on the patient's chart, by one of the members of the attending staff: "*The patient probably presents one of those cases of postcholecystectomy hyperpyrexia, of undetermined origin, which goes on to exitus.*" Routine supportive therapy, including continuous intravenous infusion of 5 per cent glucose was begun.

Six hours later (42 hours after operation), temperature had reached 107 degrees and the patient appeared moribund. On careful check-up physical examination performed at that time, heavy percussion over the lower ribs on the right side appeared to cause pain; although this point could not be ascertained accurately, because of the patient's sluggish reactions in her semicomatose state. On the faint suspicion that suppuration was present, aspiration of the subphrenic space was performed and bile stained pus was immediately encountered. Although

the patient was moribund, so that no anesthesia was necessary, incision and drainage of the subphrenic space was promptly proceeded with, in the faint hope of saving her life. A large collection of bile stained, turbid pus was evacuated, but temperature rose to 108 degrees and death occurred about 1 hour later. The following essential findings were noted at postmortem examination:

1. Defect in the common duct (due to accidental removal of a portion of one wall).
2. Ligated common and right hepatic ducts.
3. Leakage from defect in common duct, with bile peritonitis localized to the right lumbar gutter and subphrenic space.
4. Status after transdiaphragmatic drainage of right subphrenic abscess.

Culture of pus evacuated from the subphrenic space at operation, later yielded the Friedlander bacillus.

Aspiration of the subphrenic space was performed, on the basis of a single ill-defined physical sign which was noted when the patient was moribund. This sign might easily have been disregarded in view of the patient's condition; and such disregard would have resulted in adherence, before postmortem examination, to the original diagnosis. Failure to perform peritoneal aspiration or postmortem examination, probably would have resulted in the case appearing in our records as one of death from "liver shock."

CASE 3. J.B., a male, 33 years old, was admitted to The Mount Sinai Hospital with a history of having suffered three mild attacks of right upper quadrant pain, with radiation to both shoulder blades, during the preceding year. Each attack lasted 1 or 2 days, and was not accompanied by other symptoms. Five days before admission, he suffered an attack which was associated for the first time with jaundice. During the day immediately preceding admission, symptoms had begun to subside. At the time of admission, the abdomen was soft, relaxed, and not tender. Slight icterus was present. Temperature, pulse, and respiratory rate were normal. At the end of 5 days, all signs and symptoms having disappeared, X-ray films of the gall bladder were taken following the oral administration of dye. No stones were demonstrated, but the viscus failed to visualize. One week later, during which time the patient was symptom-free, operation was performed.

At operation, under general anesthesia, a moderately thick walled gall bladder containing numerous faceted stones was found. No stones could be felt in the common duct. Typical cholecystectomy, with drainage and incidental appendicectomy, was performed without difficulty. On returning to the ward, the patient was in good condition.

Twelve hours later, he was in profound shock, with a blood pressure of 40/20, temperature of 105.4 degrees, pulse rate of 140, and respiratory rate of 40. Hemoglobin was 87 per cent, and there was no clinical evidence of either intraperitoneal or external hemorrhage. The abdomen was soft and not tender. Routine anti-shock therapy, including a continuous intravenous infusion of 5 per cent glucose, was administered. Although the blood pressure rose and symptoms of shock abated to some degree, the temperature, pulse, and respiratory rate remained essentially unchanged for 4 days. At the end of that time the patient became comatose, evidence of more profound shock re-appeared, temperature rose to 107 degrees, and death occurred.

At postmortem examination, the following essential findings were noted:

1. Gangrenous bronchitis, with aspiration bronchopneumonia of both lower lobes.
2. Intraperitoneal hemorrhage, localized to the right lumbar gutter.
3. Large collection of blood, localized between the lower border of the liver and nearby adherent omentum.
4. Fat necrosis over the pancreas, omentum, and mesentery.

The pathologists considered the cause of death to be the severe pulmonary infection, and intraperitoneal hemorrhage as a contributing factor. The rôle of the fat necrosis in contributing to death, was difficult to evaluate. Aside from a mild unproductive cough which appeared on the third postoperative day, symptoms of acute respiratory disease sufficient to attract attention, were not present. The chest had been examined anteriorly and laterally on several occasions but, in view of the absence of any findings of note, the patient, who was very ill, was not turned to have his chest examined posteriorly. With failure to detect sufficient physical findings to explain the clinical syndrome, the diagnosis of "liver shock" would have seemed justified on clinical grounds had postmortem examination not been performed.

CASE 4. M.W., an obese female, 63 years of age, was admitted to The Mount Sinai Hospital with a history of mild, cramp-like, generalized abdominal pain associated with low grade fever of 6 days' duration. Vomiting had occurred only once. There had been no previous similar attacks. On admission, slight icterus was present. Temperature and pulse rate were normal. Slight tenderness without spasticity, and a small rounded mass were noted in the right upper quadrant. White blood cells numbered 12,000; polymorphonuclear leucocytes, 62 per cent. Blood pressure was 134/78.

Jaundice disappeared on the day following admission, at which time the Van den Bergh test was

normal. Blood urea nitrogen and cholesterol also were normal. During a 9 day period of observation, the patient was symptom free, and pulse and temperature remained normal. On the tenth day, operation was performed. Under general anesthesia, a large, thin walled, chronically inflamed gall bladder, containing turbid bile and several small calculi, was removed. The common duct was moderately dilated, and contained a single small calculus which was removed. The small opening made in the common duct, was closed by 3 interrupted sutures. Drainage was instituted to the liver bed and to the foramen of Winslow. Because of technical difficulties and time expended in closing a perforation accidentally made in the colon while opening the peritoneal cavity, the operative procedure lasted almost 2½ hours.

On her return to the ward, the patient's general condition appeared to be satisfactory. Sixteen hours later, temperature was 104.2 degrees, pulse rate 122, and respiratory rate 38. At that time she became quite restless. Four hours later (24 after operation), temperature was 105.4 degrees, pulse rate 144, and respiratory rate 63. The skin was cold and clammy, and the patient was irrational and in shock. In spite of vigorous therapy, she died one-half hour later with hyperpyrexia unchanged, the cause of death being entirely unexplained.

At postmortem examination the following essential findings were noted:

1. Severe hemorrhagic pneumonia of the entire right lung.
2. Marked dilatation of the stomach.
3. Coronary arteriosclerosis.
4. Adipositas cordis.

In the opinion of the pathologists, death in this elderly obese patient, was caused primarily by an extensive pneumonia of severe grade, and was contributed to by gastric dilatation. Exitus occurred in approximately 20 hours. The clinical course following operation was unexplained, and quite typical of that under discussion. Had it not been for postmortem examination, which revealed other causes, death could have been attributed to "liver shock."

DISCUSSION

The four cases presented, were selected on the basis of their conformity to the well known clinical syndrome of postcholecystectomy "liver shock." In each instance, no other diagnosis seemed possible. Subsequent postmortem examination revealed, however, that death in each case was due to unrecognized infection, either intraperitoneal or pulmonary. It may be surprising to many to note that virulent infections at various sites may produce atypical and fulminating manifestations, the causes of which are not only not recognized but not even suspected. These cases constitute the basis of our contention that the common causes of high temperature and early death cannot be excluded with finality, in suspected cases of "liver shock," without performing adequate postmortem examination. This does not mean that the usual varieties of postoperative infection cannot be recognized fairly readily, for in reviewing the hospital records it was found that not a few deaths due to infection were diagnosed clinically, the diagnosis being confirmed subsequently at autopsy.

In these cases the diagnosis was made during life on the basis of symptomatology, physical examination, laboratory data, and the characteristically irregular postoperative temperature curve; despite the fact that in several, death occurred as early as the second or third day after operation. It is of interest to note in passing that in such cases intraperitoneal infection followed operation not only in patients with obviously acute cholecystitis, but also in those in whom the clinical manifestations of cholecystitis had subsided completely or were in the process of subsiding at the time of operation. This is perhaps to be expected in view of the fact that the author in a previous communication (25) demonstrated that active infection of the gall bladder, which is usually the source of such postoperative intraperitoneal suppuration, is often present in cases in which clinical manifestations of cholecystitis are absent or minimal at the time of operation.

Connell (5) in 1931 stated that in his experience, "liver shock" in abdominal cases followed surgical procedures performed only upon the biliary tract. In other words, he believed that operations upon other intra-abdominal organs were not followed by the occurrence of this complication. Sharples concurred in this opinion. As a result of further observation, however, Connell (6) in 1934 modified his original views. At that time he reported the occurrence of six "rapid high temperature deaths" after operations such as hysterectomy, oophorectomy, appen-

dicectomy, and ventral hernioplasty. Heuer, Stanton, and Boyce and McFetridge (3) have also noted the occurrence of the syndrome of "liver shock" after operative procedures upon, and traumas to, various organs either within or outside the peritoneal cavity. Discussions, similar to those mentioned previously in regard to cases of postcholecystectomy "liver shock," have arisen in regard to these cases also. These discussions, since they do not concern us especially, will not be gone into. It is important only to point out that in this group the diagnoses recorded in the literature were made in a manner similar to those in the gall-bladder group, few adequate postmortem examinations having been performed to corroborate the clinical diagnoses.

To illustrate the importance of performing complete autopsies in suspected cases of "liver shock" in which routine postmortem examination of the abdomen and thorax are negative, the following case is presented:

E.W., a young man, 19 years old, was admitted to The Mount Sinai Hospital with a typical history of acute appendicitis of 7 hours' duration. On admission, temperature was 100.4 degrees, pulse rate 62, and respiratory rate 20. Marked tenderness and moderate spasticity were present in the right lower quadrant. The patient also was suffering from a severe acute nasopharyngitis which necessitated operation under spinal anesthesia. Nupercaine was employed as the anesthetic agent. At operation, an acutely inflamed appendix, distended with mucopus, was removed. A small amount of thin, clear, odorless fluid was present in the periappendiceal region. Appendicectomy, without drainage, was performed in the routine manner.

Following operation, the temperature immediately began to rise and several hours later reached 109.4 degrees. At that time, pulse rate was 160 and respiratory rate 48. Mild irrationality, which developed about 5 hours after operation, gave way within another 2 hours to mania that necessitated the administration of large doses of sedatives. In spite of vigorous therapy, the rapidly developing shock and hyperpyrexia could not be controlled and death occurred 14 hours after operation. (From the foregoing description, it will be seen that the clinical picture following operation, closely paralleled that observed in fulminating cases of postcholecystectomy "liver shock.")

At routine postmortem examination, the essential findings were as follows:

1. Acute congestion of all viscera.
2. Subendocardial hemorrhages.
3. Early hemorrhagic bronchopneumonia of both lungs.
4. Persistent thymus.
5. Chronic mitral valvular disease.

In the opinion of the pathologists, none of these findings was sufficient to explain the postoperative course; and the possibility of acute nupercaine (quinine) intoxication was strongly considered. *When the brain and spinal cord were examined, however, the cause of death was found to be an acute diffuse purulent meningoencephalitis.*

The foregoing case is of significance for two reasons. In the first place, it illustrates in a striking manner the necessity of performing "*complete*" postmortem examinations in all cases of suspected "liver shock," in which investigation of the abdomen and thorax proves negative. Failure to examine the brain and spinal cord, after examination of the abdomen and thorax failed to reveal significant findings, would have resulted in an entirely erroneous conception of the cause of death in this case. This is especially true in view of the fact that the actual diagnosis was not even suspected during life. The second significant point as regards the case, is that it confirms our original contention, namely, that fulminating infection, regardless of its site, is capable of producing the syndrome of so called "liver shock."

An important point to be stressed is that in every case in our records, in which the diagnosis of "liver shock" appeared warranted, subsequent postmortem examination proved such diagnosis to be erroneous. In view of the fact that cases authenticated by "complete" postmortem examination appear to have been observed by others, however, it is not justifiable to deny the existence of such an entity. At the same time, it seems only fair to state that one should be unwilling to accept the diagnosis in any case in which the findings are negative, or except for the liver are negative, unless complete postmortem studies have been performed.

In view of the observations made by the author, the validity of all diagnoses of "liver shock" which are lacking in such corroboration, is open to question. Since most of the cases reported in the literature fall into this category, it appears that in the vast majority of instances they must remain in doubt. Therefore it follows that the actual incidence of the condition cannot be stated with

accuracy, but it may be assumed to be considerably lower than has been stated by many.

It appears significant that the reported incidence of "liver shock" as a cause of death after cholecystectomy, was highest in those series in which no postmortem examinations were performed; and was lowest in those in which such examinations were performed. Thus, Neuhof and Aufses (18) in a contribution entitled "The Cause of Death after Operation," reviewed a series of eight hundred surgical deaths, followed in each instance by postmortem examination. Ninety-one of the eight hundred patients had been operated upon for diseases of the biliary system. In each case the cause of death was demonstrated readily at postmortem examination, no instance of "liver shock" being encountered. The experience of Heuer with cases of post-cholecystectomy "liver shock" has been similar; for in a recent article he writes as follows: "I have never happened to observe a death in cholecystitis without jaundice, as described by Heyd under his Type I, in which the autopsy did not reveal conditions sufficient to explain death." Judd and Parker, in a paper entitled "Mortality following Operation on the Biliary Tract, Pancreas, and Liver," report a series of 820 cholecystectomies for chronic cholecystitis. In this series there were 12 deaths, postmortem examination being performed in all. None of the deaths was found to be due to "liver shock." In concluding this discussion, a concept expressed by Dr. Damon B. Pfeiffer, and coinciding with that of the author, will be quoted. In discussing Heyd's (14) paper entitled "Liver Deaths in Surgery of the Gall-Bladder," presented at the annual session of the American Medical Association in 1931, Pfeiffer made the following statement: "It is well to appreciate the dangers that lurk in operations on individuals with a damaged liver. I should deprecate, however, the too facile adoption of such terms as 'liver shock' or 'liver death' to cover such deaths as appear mysterious and unexplainable. I suspect that some are not due to disordered hepatic chemistry, but to fulminating infection, of a sort not readily demonstrated, etc."

CLINICAL APPLICATION

Heretofore, the prognosis of a patient exhibiting the syndrome of "liver shock" has been considered to be almost invariably hopeless. Cave expressed this aptly by stating that "It is a startling and helpless situation to follow to its quick termination, one of these catastrophes, etc." It is our belief, as the result of this study, that the general attitude in regard to such cases should be modified. This is based on the demonstration that clinical manifestations may not be due to "liver shock," but may be produced by unrecognized fulminating infection. If one can demonstrate such infection to be present and institute adequate therapy, it may be possible at times to save life. It must be borne in mind, however, that an infection which produces such fulminating manifestations is indeed virulent, and demands prompt attention. Therefore it is essential, in view of the seriousness of the situation, to employ without delay every diagnostic measure that will aid in determining the presence of infection, if the latter exists, so that vigorous therapy may follow immediately.

Accordingly, the following recommendations are made in regard to patients suffering from early postcholecystectomy hyperpyrexia associated with shock of unexplained origin. The abdomen should be examined repeatedly and carefully for evidence of peritoneal irritation. Examination should include firm percussion and palpation over the lateral portions of the lower chest and costal margin. Local tenderness thus elicited, is a most valuable presumptive sign of infection of the subphrenic space; such infection together with infection of the subhepatic space, constituting the most common suppurative intra-abdominal complications of cholecystectomy. Spontaneous pain in the shoulder or tenderness on palpation in the general region of the trapezius ridge, if present, is likewise of great confirmatory significance. If no evidence of the existence of intraperitoneal suppuration can thus be found, X-ray examination should be performed. Anteroposterior and lateral films of the chest are taken at the bedside, with the patient supported in the sitting position. These films must include not only the pul-

monary fields but the diaphragms and the subphrenic regions as well. Films taken in full inspiration and expiration should be compared, for evidence of diaphragmatic immobility and elevation. Such roentgenographic studies will also definitely establish or exclude the presence of pneumonic consolidation, of sufficient extent to account for the clinical course.

In the absence of adequate pulmonary or subphrenic findings on X-ray and physical examination, exploratory peritoneal puncture (19) is indicated in an attempt to demonstrate the presence of a suppurative intraperitoneal lesion. As illustrated by Case 2, it is especially valuable in those instances in which the patient is already too ill to co-operate satisfactorily in the performance of physical examination or in the elicitation of certain important physical signs. The sites of puncture to be preferred, are points lateral to the right rectus muscle at levels somewhat above that of the umbilicus. In the event of negative results on aspiration, one should promptly aspirate the subphrenic space in the usual manner. If the patient has been operated upon under spinal anesthesia there is still one site to be investigated, if the diagnostic procedures already mentioned have failed to reveal the presence of intraperitoneal or pulmonary infection. Since suppurative meningitis without characteristic manifestations may be present (see Case 5), lumbar puncture should be performed. Gastric aspiration is recommended in all obese individuals, since unrecognized gastric dilatation in the latter at times may obscure the evidence of a suppurative lesion within the upper abdomen. The Levin tube is to be preferred for this purpose, as it can be passed with comparatively little discomfort to the patient and may be left indwelling for continuous drainage if necessary. Attention is called, also, to the value of early instituted supportive therapy, including especially the use of the continuous intravenous "drip" (16) as a means of prolonging life. Supportive therapy is of added significance, in so far as the longer the patient survives the greater is the probability of arriving at a diagnosis and perhaps of saving life.

The actual treatment of any infective lesion which may be discovered, constitutes a general surgical or medical problem depending on its nature, and need not be discussed here. Suffice it to say that treatment should be prompt and vigorous, in the hope of occasionally saving the life of a patient whose prognosis otherwise is hopeless.

SUMMARY

1. Numerous cases exhibiting a postcholecystectomy syndrome consisting of unexplained rapidly rising temperature, pulse, and respiratory rates, associated with shock and vasomotor collapse, and ending in early death, have been reported in the literature.

2. When the existence of postoperative complications such as peritonitis, hemorrhage, pneumonia, embolism, etc., are ruled out clinically and no cause of death is apparent, such a syndrome has been attributed commonly to a condition which has been termed "liver shock."

3. The diagnosis of "liver shock" in most of the cases reported in the literature was made clinically, and few adequate postmortem examinations to corroborate the diagnosis appear to have been performed.

4. Of a series of 1,360 cholecystectomies reviewed by the author, 4 cases which exhibited the typical postoperative clinical course of so called "liver shock" with unexplained fatal termination, were subjected to adequate postmortem study.

5. In each instance, the essential cause of death was found to be unrecognized fulminating intraperitoneal or pulmonary infection, no case of genuine "liver shock" being encountered.

CONCLUSIONS

1. In patients, suspected to be suffering from so called "liver shock," it is impossible during life to rule out with certainty the presence of some of the more serious postoperative complications responsible for the clinical manifestations.

2. Such complications can be excluded only by adequate postmortem examination.

3. The latter therefore constitutes the only means of corroborating the diagnosis of "liver shock."

4. Since the vast majority of diagnoses reported in the literature were made in cases which were not subjected to such examination, the former cannot be accepted with finality, and the actual incidence of "liver shock" remains in doubt.

5. The opinion of the author, based on a careful study of a small group of cases, is that genuine "liver shock" is much less common than has been assumed generally.

6. It appears that, in patients suspected to be suffering from "liver shock," unrecognized fulminating infection is the most common cause of the clinical manifestations.

7. All patients exhibiting the syndrome under discussion should be suspected of harboring virulent infection, for which early, extensive, and thorough search should be conducted during life.

8. Infection, if discovered, should be dealt with promptly and vigorously in the hope of occasionally saving the life of a patient whose outlook for recovery otherwise is hopeless.

The author is indebted to Drs. S. T. Glasser and Arthur Schifrin for permission to report the following case recently observed by them at another institution.

The patient, a woman of 47 years, was operated upon under the diagnosis of chronic cholecystitis and cholelithiasis. A small thickened gall bladder, containing many small stones, was found. Cholecystectomy with drainage and incidental appendicectomy was performed, without difficulty, under avertin oxygen ether anesthesia. Following operation the temperature, pulse, and respiratory rate began to rise progressively. In spite of vigorous therapy, temperature rose to 108 degrees, pulse to 160, and death occurred within 48 hours of operation. Before death, no satisfactory explanation could be given for the clinical manifestations.

At postmortem examination, there was found a serofibrinous peritonitis involving the operative site and the subphrenic and subhepatic spaces. On smear, the fluid contained numerous gram positive, short chained cocci and a moderate number of large gram positive bacilli. On culture, streptococci and Bacillus coli were found, the gram positive bacilli failing to grow.

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ACCIDENTS OF LOCAL ANESTHESIA

With an Experimental Study of the Toxicity of the Various Anesthetics[1]

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THE rapid increase in the use of local anesthesia has resulted in the appearance of many articles dealing with the various aspects of the subject. Except for a few details, which undoubtedly will be worked out to perfection in the near future, the technique of administration can hardly be expected to be improved. As to the anesthetics themselves, many now in use offer perfect results both as to efficiency and harmlessness, but they have one shortcoming, namely, that the duration of the effect of the administration of the drug is too brief. It is true that tragic accidents at times do occur following the use of local anesthesia and the patients suffer from serious intoxication or may even die from its use. Such untoward results are as unforeseen as a thunderbolt from a clear sky and their causes are entirely unknown. Fortunately, in view of the many thousands of operations performed under local anesthesia the world over, these discouraging accidents are exceedingly rare, but they occur often enough to warrant serious study. It is a matter of paramount importance, therefore, that reports of such complications be published in full detail and carefully registered, since it is possible to draw practical conclusions only on the basis of an extensive study and from complete statistics. In the United States a Committee for the Study of Toxic Effects of Local Anesthetics registers such accidents, and its valuable reports should be of help to all who use local anesthesia. In Europe there is as yet no similar committee. There are, however, in the European literature several articles which give a thorough and exact account of a large number of cases.

A study of these reports convinces me that these cases should be divided into two distinctly separate groups. In the first group belong those in which true intoxication results from a relative or absolute overdosage of the anesthetic. In such cases typical symptoms have been observed: psychic excitation, mental confusion, violent clonic convulsions, partial transient palsies. These symptoms may last for a rather long time, but fatal issue is uncommon. As for the rest, the symptoms tally with those observed in experimental anesthetic intoxication of animals.

In this first group belong 2 cases of Halle. Both patients received, by mistake of the pharmacist, a 5 per cent solution of procaine instead of a 0.5 per cent solution. Both were given a considerable amount, 300 cubic centimeters, i. e., 15 grams, of procaine crystals, which was injected into the soft parts of the face and neck. The patients became greatly excited and convulsions were observed, but no lasting damage resulted.

The cases of Schuberth also belong in the first group. In his first case 125 cubic centimeters of a 0.2 per cent pantocaine solution was poured into the peritoneal cavity; in the other case 175 cubic centimeters of a 0.1 per cent pantocaine solution was injected over a large field into the scalp. It is true that the dose did not exceed the safety level in either of the latter cases. However, the large, highly resorptive surface of the peritoneum and also the rich vascular supply of the scalp should have been taken into consideration. Resorption through the scalp is very rapid, especially if the anesthetic is injected over a large field. In the first case cramps were observed for 1 hour, in the second case for 25 minutes.

The symptoms in the second group of cases are in sharp contrast with those in the first group. In the second group the patient, after having received a comparatively insignificant amount of the anesthetic, suddenly develops a condition closely resembling profound collapse. The symptoms are anxiety, dizziness, paleness and/or cyanosis, cold and clammy skin, extremely feeble and running pulse, and often loss of consciousness. In about one-third of the cases muscular twitchings or even convulsions also are observed. In a rather

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great percentage death occurs within a few minutes, in spite of all therapeutic measures. Further study of these cases shows the following common factors:

1. Except in a few cases, the anesthetic used was cocaine or procaine or both. Cocaine and procaine are the drugs which have been most commonly used for the greatest number of years.

2. The amount of the anesthetic used in the overwhelming majority of cases was very small. In the case reported by E. Mayer, a patient aged 20 years, died after 6 cubic centimeter of a 0.5 per cent solution of procaine was given for a tonsillectomy. In another case of his the patient died after the injection of 12 cubic centimeters of a similar solution for an operation for hemorrhoids. In one case of Halle—a tonsillectomy—5 cubic centimeters of a 0.5 per cent procaine solution caused death. Schoemaker observed sudden death after the administration of 2.5 cubic centimeters of a 0.5 per cent procaine solution for epigastric hernia. In general the amount of procaine employed ranged from 0.01 to 1.1 grams.

3. The concentration never exceeded the generally accepted limits; it amounted, in 90 per cent of all cases, to from 0.5 to 1 per cent. This has been verified in many cases by subsequent chemical examination of the fluid used.

4. The amount of epinephrine used never exceeded the generally accepted dosage. Much heavier dosages are administered to patients suffering from bronchial asthma and other allergic conditions without the slightest inconvenience.

5. Curiously enough, more than the half of all accidents occurred with operations on the neck and two-thirds of these were tonsillectomies. The others were chiefly splanchnic. spinal, and sacral anesthesias.

6. In a relatively great percentage of cases necropsy showed persistent thymus gland or severe myocardial damage. There were, however, many entirely negative findings.

What is the cause of these unexpected and unforeseen tragedies? Overdosage, intoxication in the strict sense of the word, can be ruled out, the dosage employed being but an insignificant fraction of the normally tolerated dose. As to accidental intravenous injection, there is no doubt that the passing of a greater amount of anesthetic into a vein may cause serious intoxication or even immediate death. Therefore, de Takats recommends great caution in infiltrating highly vascular regions (varicosities, hemorrhoids, deep regions of the neck). In the cases in question, however, such small doses have been used that they could not possibly have caused intoxication, even if the full amount had directly entered a vein. Hackenbruch himself says that a few cubic centimeters of anesthetic injected into a vein does not cause any harm. Moreover, it is well known that the intravenous lethal dose of anesthetics belonging in the aminobenzoylic ester group (procaine, tutocaine, pantocaine) amounts to one-tenth of the subcutaneous lethal dose. It is evident that much greater doses are tolerable intravenously than the doses in question. Epinephrine intoxication may be considered, its symptoms being to a certain extent similar yet not identical. This question has not received sufficient study as yet. As to the possibility of hypersensitiveness —idiosyncrasy, some allergy-like condition— it must be admitted that some patients are known to be hypersensitive to local anesthetics. In a number of accidents reported the symptoms, too, were suggestive of anaphylactic reaction. However, this point has not as yet been sufficiently investigated. Systematic skin sensitivity tests were not made. Very interesting is Seeger's case of apparently acquired hypersensitiveness. The patient died within a few minutes after the administration of a small quantity of the same local anesthetic which at the occasion of a previous operation was well tolerated in a much heavier dosage. If we accept the theory of hypersusceptibility, the case mentioned is an example of sensitization by previous exposure, similar to acquired protein allergy.

In an attempt to explain the accidents of local anesthesia Seeger, takes as a starting point the fact that most fatalities occur with operations on the neck. He believes that this is due to anatomical causes. On the neck within a narrow space there are crowded together organs of immediate vital importance —vagus nerve, sympathetic ganglia, the

carotid sinus—which can be damaged by the anesthetic in different ways. First, the anesthetic may anesthetize or paralyze them by direct diffusion and in this way cause serious disturbances in the organs supplied. The great irritability of the denervated heart, e.g., is well known. Second, pressure produced by the injected solution or the result of a hematoma caused by the inadvertent puncture of a vessel in this highly sensitive region may cause sudden catastrophe. In the case of Wiemann there was found, at the site of the injection, a hematoma which compressed the vagus nerve and the upper cervical ganglion. Injury to the vertebral or the carotid artery is another possibility. Should the fluid be injected inadvertently into an artery, the brain may become flooded with a concentrated anesthetic solution. Moreover, in forensic medicine many cases are recorded of immediate death following blows and other injuries to the neck. Accidents after local anesthesia in other regions cannot be satisfactorily explained on the basis of these deliberations, however. Seeger believes that in general these accidents are caused by some reflex inhibition, the result of a mere physical traumatism. That psychic disturbances, too, are liable to play an important part is shown by one case of Halle—the patient collapsed just before the starting of the anesthesia and went into serious shock. If this had happened after the anesthetic had been administered, there would have been not the slightest doubt that the collapse was caused by the anesthesia.

From the facts mentioned it does not seem justifiable to attribute the accidents belonging in the second group to intoxication; they ought to be regarded rather as instances of a kind of acute shock. As to the mechanism of the latter, let us state that it is not well understood. Allergy-like hypersensitiveness probably plays a rôle in at least some of the cases.

The pathology of those mild intoxications, the symptomatology of which consists of transitory anxiety, palpitation, and sweating, is also unexplained. It seems to me that they are due to a specific procaine effect. At any rate, since we discontinued the use of procaine at the Third Surgical Unit of the University of Budapest and began to use, first, tutocaine, later nupercaine, and at present pantocaine, we have not observed a single case of such untoward result in a series of more than 15,000 major operations.

Therefore with our present knowledge we have not much hope meanwhile of becoming able to prevent or to obviate fatalities belonging in the second group, except perhaps by the use of immediate barbital therapy, the results of which seem to be encouraging. True intoxications belonging in the first group, however, can and should be prevented. The more extensive use and perfected technique of local anesthesia has resulted in its use in the performance of operations of longer duration and greater extent. The performance of these extensive operations often necessitates the use of such large amounts of anesthetic solution that the problem of intoxication due to local anesthetics will probably soon come into the foreground of interest. Therefore we have found it worth while to study by animal experiments several factors regarding dosage which may influence our knowledge as to the toxicity of local anesthetics. We investigated the following three questions: What is the influence of local anesthetics on toxic effects in relation to (1) concentration of the solution employed, (2) the site of subcutaneous injection, and (3) the protracted fractional administration of the anesthetic.

The literature on these three questions is rather scanty. We could not find a single paper dealing with a systematic study of the problem; we found only parenthetical remarks concerning this topic. According to Haertel the lethal dose administered in a given concentration will not cause death if it is not injected at once but fractionally over a short period of time; a dose lethal in a given concentration will not be lethal if administered in a more diluted solution; data as to the lethal dose of an anesthetic are to be depended upon only if they contain three items: amount, concentration, and method of administration. Haertel does not mention the rôle of the site of injection. Ádám, on the basis of his experiences with a vast surgical material, has come to the conclusion that the toxicity of a local anesthetic is decreased by the use of highly diluted solutions, by injecting them far from the

central nervous system and by the fractional administration of the amount required; on the other hand he believes that high concentrations of the solution, injection near the central nervous system, and the sudden flooding of the organism with great doses increases the toxic effects. Pouchet injected 40 milligrams of cocaine dissolved in 1 cubic centimeter of water into the peritoneal cavity of a guinea pig and it died; another guinea pig received 100 milligrams dissolved in 15 cubic centimeters of water, and it survived.

According to Zunz the toxicity of procaine depends on the concentration: of a 1 per cent solution not more than 1.25 grams, of a 2 per cent solution not more than 0.75 gram should be employed. It is advisable to use a 0.5 per cent solution. *Toxikologie* by Starkenstein, Rost, and Pohl mentions only that concentrated solutions are quickly resorbed, whereas diluted solutions are bound locally. In the experiment of Braun, a rabbit suffered severe intoxication from 0.005 gram of cocaine in a 10 per cent solution injected into the ear vein, whereas it tolerated four times the dose mentioned if injected in a 0.1 per cent solution. He does not mention the speed of the injection, which in our opinion probably played the major part. The data mentioned seem to show that concentration has a significant influence on toxicity. On the contrary, according to Martin the lethal dose of procaine for the dog is 300 milligrams per kilogram of body weight, a 10 per cent solution being used. This exactly equals the lethal dose if a 1 to 2 per cent solution is used. Veterinary surgeons use chloral hydrate extensively for intravenous injection, in 5 to 20 per cent solutions. The efficient dose is independent of the concentration (Marcenac, Weischer). There is no doubt that fractional administration greatly reduces toxicity. According to Schulemann a quadruple lethal dose of tutocaine may be safely injected into the ear vein of a rabbit if it is administered at a slow rate.

In our experiments we studied four local anesthetics: procaine, tutocaine, nupercaine, and pantocaine.

Concerning procaine, it should be mentioned that both non-proprietary procaine and original novocain of the German firm I. G. Farbenindustrie have been assayed, the two being of identical chemical formula. We found no difference whatever in their action. Of tutocaine we used the original 0.5 gram tablets of the I. G. Farbenindustrie, labelled T III. Concerning pantocaine we tried both the 0.1 gram tablets and pantocaine crystals. We did this because on checking the weight of the tablets we found that their average weight was 0.14 gram. In replying to our question the firm stated that this excess of weight was due to inert binding substance. This statement has been proved to be correct in our experiments. Nupercaine was used in crystalline form. Concentrated solutions of the latter (1 to 2 per cent), irrespective of whether prepared with physiologic salt solution or with distilled water are liable to show heavy turbidity on standing for a few minutes and quite soon a crystalline precipitate forms. We do not know the cause of this phenomenon—perhaps the presence of traces of alkali—but at all events we injected the solutions before they had time to become turbid. As for the rest, all solutions have been freshly prepared with a 0.8 per cent solution of sodium chloride. No addition of epinephrine was used because it seemed to us undesirable to be obliged to take into account the toxic action of another, by no means, indifferent substance. On the other hand, epinephrine retards the rate resorption in an incalculable measure.

We started our experiments by determining the minimal lethal dose of the four compounds mentioned. Though these data are to be found in the literature, they are not entirely uniform; therefore it seemed to us expedient to determine them once more. These introductory experiments have been performed with solutions of a standard strength (2 per cent) of all the anesthetics to be assayed and only after this were solutions of different concentrations tried. The injections were made into the subcutaneous tissue of the lower abdomen or the inguinal region, respectively, at one site, forming a circumscribed deposit. The same animal was not used twice within a period of at least 5 days. Each dose was run with 5 animals. The dose which caused the death of at least 3 animals in 5 used was arbitrarily accepted as the minimal lethal dose. We noted not only the fact of death, but also the time which elapsed between the injection and death. In the beginning we used white rats, body weight from 110 to 180 grams. It soon became evident, however, that this species is so insensitive, so tolerant to local anesthetics, that the introduction of the lethal dose in more diluted solutions would have

been impossible on account of the enormous quantity of fluid necessitated. When 2 per cent solutions were used we found the following lethal doses:

Procaine: 2400 milligrams or 120 cubic centimeters per kilogram body weight.
Tutocaine: 700 milligrams or 35 cubic centimeters per kilogram body weight.
Pantocaine: 80 milligrams or 4 cubic centimeters per kilogram body weight.
Nupercaine: 70 milligrams or 3.5 cubic centimeters per kilogram body weight.

Consequently 240 cubic centimeters of a 1 per cent procaine solution or 350 cubic centimeters of a 0.2 per cent tutocaine solution per kilogram of body weight would have been the approximate lethal dose. This amount of fluid would have been so heavy a burden to the circulation, if injected parenterally, that it would have made valueless the results of the experiments. Therefore, we later took guinea pigs because this species is much more sensitive to local anesthetics. The course of the intoxication is quite similar in both species. It will be described as it is shown in the guinea pig, mention being made also of the differences observed. The body weights of the guinea pigs employed ranged from 165 to 740 grams. We did not observe any difference in sensitivity as related to on body weight.

The symptoms of intoxication from procaine, tutocaine, and pantocaine are quite similar. Depending on the dose, after a latency period of from 4 to 20 minutes the animals will begin to tremble and to stagger, and there is a slow nodding movement of their heads. At the same time they will drag their hind extremities. After 1 to 2 minutes the animals, apparently lame, will turn on their sides and lie motionless. After another few minutes violent convulsions will start. The head is spastically bent backward, there is an opisthotonos-like stretching of the entire body. The extremities perform quick, jerky movements, which, on the whole, seem rather coordinated and resemble running. At times the spasms subside only to start anew after a few seconds. Often curious twisting, spiral movements of the head are observed. The convulsions often are violent enough literally to throw the animals from their baskets. Later, the convulsions gradually subside and paralytic symptoms become dominant. The animals will lie motionless, with respiration as the only sign of life. Later the rate of respiration rapidly decreases and it becomes stridulous, possibly due to spasm of the glottis. This condition lasts for a variable length of time. In general the animals die within 20 minutes, or there is a reverse succession of the symptoms mentioned with ultimate complete recovery. In about 90 per cent of the cases, the entire course of the intoxication is about 1½ hours or less, whether the animal dies or recovers. However, a few instances of death occurred after more than 3 hours.

Nupercaine intoxication shows a certain departure from the type described. The first symptom to be observed is violent psychomotor excitation. The animals leap about, snap at all objects within their reach, nibble in an excited way, yell in a curious agitation. Very soon, however, they become paralyzed and later go into convulsions. The further course of intoxication is very similar to that observed with the aminobenzoylic esters, with the only exception that on recovery there is again a stage of motor excitation. In rats, all anesthetics caused identical reactions, quite similar to procaine intoxication of the guinea pig, the convulsions, however, being less violent.

The experimental data reported in Table I concern guinea pigs.

INFLUENCE OF SITE OF INJECTION ON THE TOXICITY OF LOCAL ANESTHETICS

In these experiments we employed a 2 per cent solution of pantocaine, the minimal lethal dose of which has been found in our previous experiments to be 1.0 cubic centimeter per kilogram body weight if injected into the subcutis of the lower abdomen. One-third of this amount—0.33 cubic centimeter per kilogram—has been injected subcutaneously into the submandibular region of 5 guinea pigs. No animal died; we did not even observe a single case of somewhat serious intoxication. Therefore, another 5 guinea pigs were similarly injected with twice this amount—0.66 cubic centimeter per kilogram. One of these animals died after 70 minutes,

TABLE I.—INFLUENCE OF DEGREE OF DILUTION ON THE TOXICITY OF LOCAL ANESTHETICS

1. PROCAINE

2 per cent solution

0.40 gm. = 20 c.cm. per kgm.

470	9,4	10 minutes later	C	□	
220	4,4	12 minutes later	C	□	
360	7,2	10 minutes later	C	□	
450	9,0	14 minutes later	C	□	
460	9,2	8 minutes later	CC	□	

0.45 gm. = 22.5 c.cm. per kgm.

490	11,0	15 minutes later	CC	□	
490	11,0	10 minutes later	CC	□	
510	11,5	10 minutes later	CC	□	
540	12,2	16 minutes later	CC	+	beyond 2 hours
500	11,3	14 minutes later	CC	□	

0.50 gm. = 25 c.cm. per kgm.

430	10,7	10 minutes later	CC	+	after 4 hours
470	11,7	10 minutes later	CC	□	
560	14,0	10 minutes later	CC	+	after 1 hour
400	10,0	14 minutes later	CC	+	after 84 minutes
510	12,8	12 minutes later	CC	□	

10 per cent solution

0.40 gm. = 4 c.cm. per kgm.

460	1,84	12 minutes later	CC	□	
410	1,64	11 minutes later	CC	□	
560	2,24	10 minutes later	CC	□	
500	2,0	10 minutes later	CC	+	after 90 minutes
530	2,1	11 minutes later	CC	□	

0.45 gm. = 4.5 c.cm. per kgm.

440	2,0	10 minutes later	CC	+	after 70 minutes
710	3,2	11 minutes later	CC	□	
600	2,7	10 minutes later	CC	+	after 90 minutes
540	2,4	9 minutes later	CC	+	after 46 minutes
520	2,3	14 minutes later	CC	□	

2. TUTOCAINE

2 per cent solution

0.15 gm. = 7.5 c.cm. per kgm.

480	3,6	25 minutes later	CC	□	
430	3,2	10 minutes later	CC	□	
490	3,7	10 minutes later	CC	□	
630	4,7	12 minutes later	CC	+	after 90 minutes
450	3,4	18 minutes later	CC	□	

0.175 gm. = 8.75 c.cm. per kgm.

450	3,9	10 minutes later	CC	+	after 56 minutes
450	3,9	10 minutes later	CC	+	after 40 minutes
470	4,1	10 minutes later	CC	□	
540	4,7	12 minutes later	CC	□	
580	5,1	5 minutes later	CC	+	after 1 hour

1 per cent solution

0.10 gm. = 2 c.cm. per kgm.

610	1,22	ϕ		□	
600	1,20	10 minutes later	CC	□	
510	1,02	15 minutes later	C	□	
510	1,02	25 minutes later	P,C	□	
620	1,24	25 minutes later	P,C	□	

0.125 gm. = 2.5 c.cm. per kgm.

460	1,15	8 minutes later	CC	+	after 1 hour
440	1,1	11 minutes later	C	□	
550	1,6	7 minutes later	CC	+	after 55 minutes
380	0,95	9 minutes later	CC	□	
520	1,3	12 minutes later	CC	□	

0.15 gm. = 3 c.cm. per kgm.

190	0,57	5 minutes later	CC	+	after 30 minutes
190	0,57	5 minutes later	CC	+	beyond 3 hours
620	1,86	5 minutes later	CC	+	after 45 minutes
590	1,77	30 minutes later	CC	+	after 55 minutes
520	1,56	16 minutes later	CC	+	after 50 minutes

Explanation of signs: +died, □survived, C convulsions, CC violent convulsions, P paralysis, E psychomotor excitation. The first column of numbers shows the weight of the animals in grams, the second one shows the amount of solution injected in cubic centimeters.

0.5 per cent solution

0.15 gm. = 30 c.cm. per kgm.

165	4,9	15 minutes later	P	+	beyond 3 hours
200	6,0	10 minutes later	C	□	
580	17,4	45 minutes later	P	□	
700	21,0	ϕ		□	
440	13,2	30 minutes later	C	□	

0.20 gm. = 40 c.cm. per kgm.

250	10,0	5 minutes later	P	+	after 5 hours
480	19,2	20 minutes later	CC	□	
510	20,4	13 minutes later	CC	+	after 30 minutes
590	23,6	15 minutes later	CC	□	
470	18,8	45 minutes later	P	□	

0.225 gm. = 45 c.cm. per kgm.

390	17,6	10 minutes later	CC	□	
570	25,7	20 minutes later	P,C	+	after 1 hour
360	16,2	16 minutes later	CC	+	after 54 minutes
540	24,3	11 minutes later	P,C	+	after 38 minutes
520	23,4	16 minutes later	C	□	

3. PANTOCAINE

2 per cent solution

0.015 gm. = 0.75 c.cm. per kgm.

630	0,46	17 minutes later	P,C	□	
710	0,53	17 minutes later	C	□	
740	0,57	11 minutes later	P,C	+	after 22 minutes
650	0,47	10 minutes later	P	□	
360	0,27	5 minutes later	P,C	□	

0.02 gm. = 1.0 c.cm. per kgm.

710	0,71	6 minutes later	C	+	after 32 minutes
610	0,61	6 minutes later	C	+	after 20 minutes
490	0,49	7 minutes later	CC	+	after 28 minutes
410	0,41	9 minutes later	CC	□	
520	0,52	8 minutes later	CC	□	

0.1 per cent solution

0.02 gm. = 20 c.cm. per kgm.

550	11,0	15 minutes later	C	+	after 1 hour
610	12,2	15 minutes later	C	□	
570	11,4	ϕ		□	
410	8,2	8 minutes later	CC	+	after 40 minutes
370	7,4	30 minutes later	P	□	

0.025 gm. = 25 c.cm. per kgm.

710	17,7	6 minutes later	C	□	
480	12,0	8 minutes later	C	□	
560	14,0	5 minutes later	C	+	after 24 minutes
550	13,8	4 minutes later	C	+	after 30 minutes
200	5,0	10 minutes later	C	+	after 70 minutes

0.03 gm. = 30 c.cm. per kgm.

340	10,2	5 minutes later	CC	+	after 30 minutes
470	14,1	10 minutes later	CC	+	after 40 minutes
480	14,4	10 minutes later	CC	+	after 50 minutes
320	9,6	10 minutes later	CC	+	after 36 minutes

4. NUPERCAINE

2 per cent solution

0.012 gm. = 0.6 c.cm. per kgm.

640	0,38	30 minutes later	E,C	□	
500	0,30	18 minutes later	E,C	□	
520	0,31	26 minutes later	E,C,P	□	
200	0,12	17 minutes later	E,C	□	
600	0,36	19 minutes later	E,C	□	

0.015 gm. = 0.75 c.cm. per kgm.

590	0,44	8 minutes later staggering	E,C	□	
600	0,45	5 minutes later	CP	+	after 50 minute
370	0,28	10 minutes later	C	□	
560	0,42	8 minutes later	C	□	
500	0,38	12 minutes later	C	□	

0.020 gm. = 1.0 c.cm. per kgm.

460	0,46	28 minutes later	E	□	
530	0,53	15 minutes later	E,C	□	
740	0,74	6 minutes later	E,C	+	after 34 minutes
580	0,58	8 minutes later	E,C	+	after 44 minutes
500	0,50	12 minutes later	E,CC	□	

0.025 gm. = 1.25 c.cm. per kgm.

550	0,69	8 minutes later	C	+	after 80 minutes
500	0,63	6 minutes later	C	+	after 44 minutes
440	0,55	6 minutes later	C	+	after 28 minutes
420	0,40	11 minutes later	C	+	after 56 minutes
420	0,53	7 minutes later	C	□	

0.5 per cent solution

0.015 gm. = 3 c.cm. per kgm.

700	2,1	8 minutes later staggering		□	
420	1,3	14 minutes later staggering	E	□	
570	1,7	ϕ		□	
650	1,95	6 minutes later	E,CC	+	
630	1,6	ϕ		□	

0.02 gm. = 4 c.cm. per kgm.

590	2,36	6 minutes later staggering	E,C	+	after 46 minutes
520	2,1	8 minutes later staggering	CC	+	after 40 minutes
480	1,9	14 minutes later staggering	CC	□	
380	1,5	17 minutes later	CC	□	
640	2,6	7 minutes later	P,C	+	after 36 minutes

0.1 per cent solution

0.015 gm. = 15 c.cm. per kgm.

420	6,3	20 minutes later staggering		□	
500	7,5	24 minutes later staggering	E,C	□	
470	7,1	16 minutes later staggering		□	
500	7,5	ϕ		□	
560	8,4	18 minutes later	CC	+	after 70 minutes

0.020 gm. = 20 c.cm. per kgm.

520	10,4	12 minutes later	E,C	+	after 36 minutes
530	10,6	10 minutes later	E,C	+	after 40 minutes
710	14,2	14 minutes later	E,C	□	
560	11,2	12 minutes later	E,C	+	after 44 minutes
400	8,0	18 minutes later	E,C	□	

the 4 others showed mild spastic and paralytic symptoms. Since it has been unequivocally demonstrated by these few experiments that the site of injection does not noticeably influence the toxic action, we discontinued our investigations in this direction.

INFLUENCE OF PROTRACTED FRACTIONAL ADMINISTRATION ON THE TOXICITY OF LOCAL ANESTHETICS

In these investigations we employed a 0.1 per cent pantocaine solution, the minimal lethal dose of which was found in our previous experiments to be 25 cubic centimeters per kilogram of body weight. We took 7 guinea pigs, weighing from 480 to 710 grams. They were injected each with 5 cubic centimeters of the solution mentioned, every 20 minutes. The experiment was continued for 2½ hours, during which time each guinea pig received 9 injections, totalling 45 cubic centimeters. This is four times the lethal dose of the smallest animal and almost three times the lethal dose of the heaviest animal. In spite of this only 3 animals showed mild symptoms of intoxication — muscular hypotonia, abortive cramps—the others did not seem ill at all. One hour and a half after the completion of the experiment all animals were quite alert.

RECAPITULATION

A survey of the tables shows the following results:

1. The toxicity of the anesthetic compounds assayed does not completely tally with data of the literature. We do not speak of the surprisingly high lethal doses observed with white rats, as no corresponding data in the literature are available. As to guinea pigs the generally accepted lethal doses on subcutaneous injection are: procaine, 400; tutocaine, 200, pantocaine, 30 to 40; and nupercaine, 10 milligrams per kilogram of body weight. Concerning procaine and tutocaine, our experiments confirm these data, whereas we found pantocaine more toxic and nupercaine less toxic than is generally accepted. The lethal dose of both pantocaine and nupercaine has been found to be 20 to 25 milligrams per kilogram of body weight. According to the hitherto accepted data, the absolute toxicities of procaine, tutocaine, pantocaine, and nupercaine are as 1:2:15:40, whereas their therapeutic indexes are, considering that the anesthetic power of a 1 per cent procaine, a 0.2 per cent tutocaine and a 0.1 per cent either pantocaine or nupercaine solution is equal, as 1:0.4:1.5:4. (Here the term therapeutic index means the relation of the efficient concentration to the minimal lethal dose, procaine being taken as the unit.) According to our results the relation of the absolute toxicities of the compounds mentioned is as 1:2.5:22:22, whereas that of their therapeutic indexes is as 1:0.5:2.2:2.2. Consequently, as to toxicity, tutocaine is to be considered the most suitable local anesthetic. Then follows procaine and the highest toxicity is exhibited by both pantocaine and nupercaine. Of course, only the lethal doses have been used as a basis of comparison and not the other advantages or drawbacks.

2. The degree of dilution apparently does not materially affect toxicity, at least not in animal experiments. The greatest difference in toxicity observed with solutions of different concentration of the same anesthetic—5 and 0.5 per cent solution, respectively, of tutocaine—did not exceed 30 per cent. This is almost within the limits of observational faults and may be practically neglected. At

first glance this result is somewhat surprising, as it could be expected that more concentrated solutions, because of their quicker resorption, will show a higher toxicity. On more thorough consideration, however, of the factors involved in and influencing the toxicity of a given agent, it becomes evident that their different concentrations may yield widely divergent results. First, it is rather questionable whether the resorption of a concentrated anesthetic solution is really markedly quicker than that of a more diluted one. It should be borne in mind that even the most concentrated anesthetic solutions in use are highly hypotonic, as far as the anesthetic compound itself is concerned. The molecular size of tutocaine, for example, is 286, therefore an isotonic solution would have the strength of almost 5 per cent. Our routine solutions are much weaker. The relatively quicker diffusion of a small volume of a more concentrated solution may also become counterbalanced by the larger surface of a greater quantity of the more diluted solution. The importance of the size of the resorptive surface need not be stressed. It is exceedingly difficult to perform exact experiments in this respect. In the course of our investigations we injected 2 guinea pigs with half the lethal dose of a 0.5 per cent tutocaine solution into the subcutis of the abdomen, over as large an area as possible. Both animals died within 45 minutes. Besides this, the concentration in the blood of any given poison is influenced by the proportion between the rates of resorption and of detoxification or excretion, respectively. Local anesthetics are quickly detoxicated and neutralized by the organism. A rabbit, for example, is able to neutralize 3 milligrams of procaine or 0.15 milligram of pantocaine each minute per kilogram of body weight (H. Schmidt). In this way the full lethal dose is made harmless in about 2 hours. With so quick a neutralization, it seems to be open to doubt whether a moderate acceleration of resorption will constitute an actual danger. Moreover, the toxic action of any agent does not exclusively depend on its concentration in the blood. Of course, there are poisons the toxic action of which is directly proportional to their concentration in the blood—most of the narcotics—with other poisons, however, it depends on the product of concentration and duration of action. This means that a lower concentration, if it acts for a sufficient length of time, may produce the same effect as a higher concentration acting for a shorter time (Starkenstein-Rost-Pohl). This phenomenon is caused by the fact that it takes a certain length of time for the cells to store an efficient amount of poison from the surrounding fluids (elective fixation, storage, cumulation). In this way a more diluted solution if it is being resorbed over a longer period of time may, under certain circumstances, prove even more harmful. Moreover, a cell showing greater avidity for a certain poison is not necessarily the more sensitive one. It is even possible that by increasing the concentration such cells will be compelled to take up greater amounts of the poison—cells of liver, muscle, kidneys—which are less susceptible to injury by it and in this way the highly sensitive nerve cells will actually be spared. It need not be emphasized that this is possible only within certain limits which are determined by a favorable or unfavorable relation between the rates of resorption, detoxication, and excretion, cumulation and many other factors, a part of which are meanwhile beyond the range of being understood. As a matter of fact, in animal experiments, the constellation of these factors is such that the influence of concentration upon toxicity cannot be demonstrated. As to human beings, we do not wish at this time to draw positive inferences.

3. That the site of the subcutaneous injection is not a main factor is not surprising if resorption takes place exclusively into blood channels, although on the neck resorption is probably quicker because of its abundant blood supply. If resorption were to take place by way of lymphatics too, resorption would be quicker from sites connected by a short route with the thoracic duct. At any rate, the ultimate differences are so slight that they are entirely overcome by the levelling activity of the organism. Here we do not deal with the danger of direct diffusion into the central nervous system if the anesthetic is injected too near to the spine, as this is not a problem of toxic action in the pharmacological sense of

the word. The curious frequency of fatalities following operations on the neck done with local anesthesia has been discussed already in the early part of this paper.

4. Protracted fractional administration greatly reduces the toxic action of local anesthetics as could be foreseen from data gleaned from the literature and from knowledge concerning the pharmacology of the compounds in question.

As stated, we do not maintain that our results positively apply to human beings. The administration of small doses even of concentrated solutions, if necessary, is probably safe. If, however, large quantities are to be used, the diluted solutions are advisable, since among other dangers, that of overdosage is thus minimized. Moreover, it is objectionable to charge the organism with a heavier load of poison than is strictly necessary, however mild this poison may be. It seems to be expedient, too, if a considerable amount of anesthetic solution is required, not to administer it at once, but rather in fractional dosages.

SUMMARY

1. Accidents of local anesthesia are to be divided into two groups: (a) true intoxication resulting from overdosage, and (b) acute shock, the pathological mechanism of which is not well understood.

2. In animal experiments, variation of the degree of dilution and of the site of subcutaneous injection did not noticeably influence the toxic action of local anesthetics, whereas fractional administration of a total of three to four times the minimal lethal dose over a period of 2½ hours was tolerated by the animals without any serious untoward effect.

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CLINICAL SURGERY

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JEJUNOSTOMY AS A PALLIATIVE PROCEDURE IN INOPERABLE OBSTRUCTIVE CARCINOMA OF THE STOMACH

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JEJUNOSTOMY, which is the creation of an artificial opening in the upper part of the jejunum for the introduction of nourishment, is a procedure which is occasionally useful in inoperable obstructive carcinoma of the stomach. It is a short and simple operation which can be done under any type of anesthesia, though the writer's preference is for nitrous oxide and oxygen or ethylene anesthesia. The decision as to the agent to be employed depends chiefly upon the patient's condition and the surgeon's own desires.

The operation is performed in the following steps: (1) incision of the abdomen, (2) exploration of the abdomen, (3) identification and exteriorization of the jejunum, (4) definition of the groove or channel in which the jejunostomy tube is to lie, (5) insertion and infolding of the jejunostomy tube, (6) closure of the abdominal wall.

1. The abdomen is opened through a left paramedian incision, about 6 inches long, the lower limit of which is on a level with the umbilicus. A median incision may be used, but an incision slightly more to the left gives a better exposure of the jejunum, which occupies the left hypogastrium, and permits a more satisfactory exploration of the abdominal contents.

2. A careful exploration of the entire abdomen should not be omitted in any case in which the patient's condition warrants the additional time, even though all the clinical and laboratory evidence should indicate that no procedure other than jejunostomy is possible. Jejunostomy, as we shall point out later, is frankly a last resort, and while it is definitely indicated in a small number of cases, it should never be done until a careful exploration has made it clear that no other procedure is feasible.

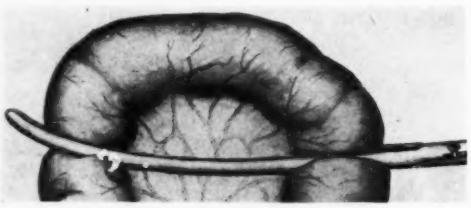

Fig. 1. Jejunum held out of wound by intestinal clamps. (Modified from Bickham.)

3. The upper 12 inches of the jejunum is now sought for and identified. This portion lies just distal to the duodenojejunal junction and is easily identified by its relation to this landmark and to the ligament of Treitz, as well as by its position in relation to the second lumbar vertebra, to the left of which it lies. As soon as the bowel is brought up into the wound, the root of the mesentery is palpated, according to the method of Monks, to determine that there is no twist in the mesentery. This precaution is exceedingly important; if the bowel should be twisted, and that fact should not be discovered, the jejunostomy tube would be inserted in the wrong direction and feeding would be impossible. Following this investigation, and the untwisting of the bowel if that should prove necessary, the portion of the jejunum in which the operation is to be done is held out of the wound (Fig. 1) by an intestinal clamp, preferably rubber-covered, with a soft spring, which is so applied as to extend well beyond the operative field. The bowel is then surrounded by gauze packs which have been dipped in warm saline solution.

4. The groove in which the jejunostomy tube is to lie is indicated on the antimesenteric wall of the gut by the application of Allis forceps, or, better, by long traction sutures of silk (Fig. 2). Sutures do less damage to the bowel wall, and are useful later in fastening the jejunostomy tube in position. The groove in which the tube is to lie should be at least 4 inches long; the longer it is, the more securely is the tube held in place and the less likely is leakage to occur.

5. A stab wound half an inch long is made into the intestinal lumen 1 inch above the lower trac-

Fig. 2.

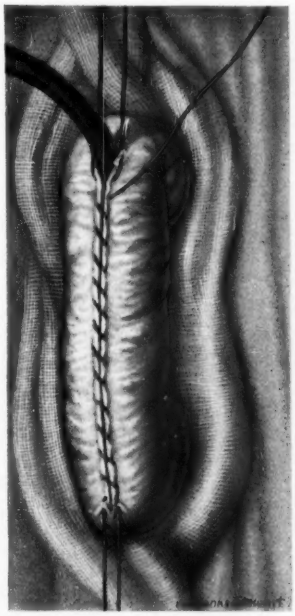

Fig. 3.

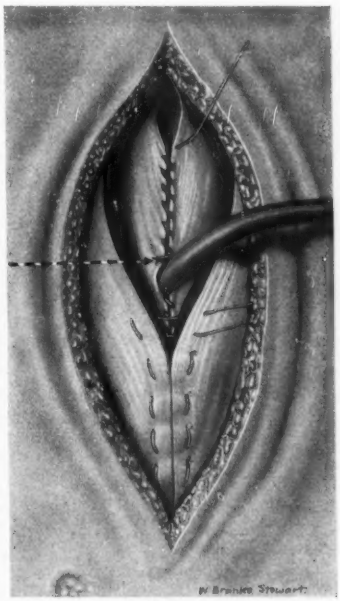

Fig. 4.

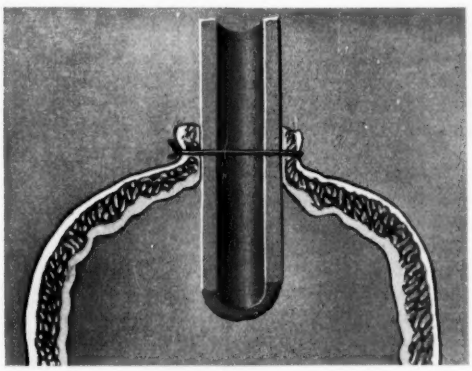

Fig. 2a.

Fig. 3a.

Fig. 2. Tube lying on wall of jejunum, in groove outlined by upper and lower traction sutures held on tension, after it has been inserted into lumen of bowel and fastened by transfixion suture. a, Cross section of jejunum, showing tube inserted into lumen and fastened in place by transfixion suture.

Fig. 3. Tube buried in groove formed by fold of jejunal wall. Burial accomplished by continuous Lembert sutures. a, Cross section showing the tube buried in the wall of the jejunum.

Fig. 4. Closure of peritoneum and fascia after fixation of jejunum to peritoneum by upper traction suture (indicated by arrow). Note special mattress sutures of silk to close aponeurosis of rectus muscle.

tion suture. The opening must be sufficiently large to permit the entrance of a No. 16 French catheter, but not large enough to permit leakage about it. The tip of the catheter is inserted into the stab wound and is pushed down into the intestinal lumen (Fig. 2a), parallel with the intestinal wall, for 2 inches or more. It is held in place at the point of insertion (Figs. 2 and 2a) by a plain No. 0 catgut suture which transfixes both the bowel wall and the tube. By the time this suture has been absorbed, the opening has accommodated itself to the size and shape of the tube.

The tube, as it makes its exit from the stab wound (Fig. 2) lies along the surface of the intestine and passes through the untied ends of the upper traction suture. Both the upper and lower

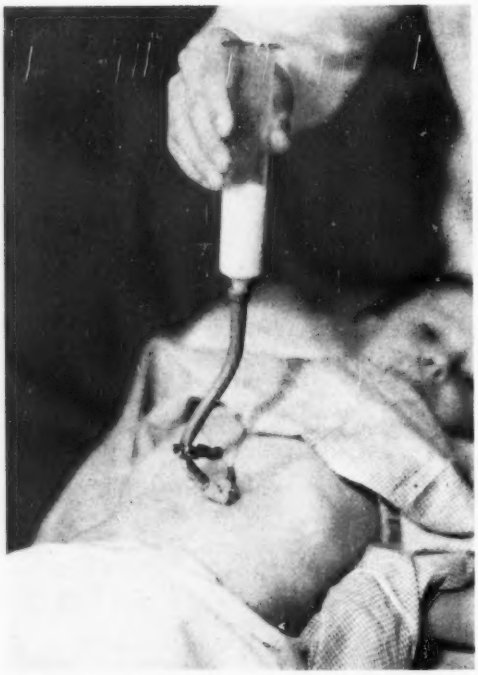

Fig. 5. Introduction of nourishment by Triumph syringe, applicable to jejunostomy or gastrostomy. Note stopcock on tube, which is closed except when nourishment is being introduced.

traction sutures are now held on tension, and as a result of this maneuver there is formed a channel or groove in which the catheter lies. The ridges forming the sides of this groove are whipped together at the top over the catheter, with a continuous Lembert suture of silk (Figs. 3 and 3a). The serosal coat of the intestine thus forms a snug channel in which the catheter lies. The infolding is carried down well beyond the point of entry of the catheter, so that any leakage into the abdominal cavity is guarded against. The lower traction suture is now tied and cut. The upper suture is passed through the peritoneum, the transversalis fascia, and the posterior sheath of the rectus muscle before it is also tied and cut. By this transfixion stitch the upper end of the intestinal channel is attached to the peritoneal surface of the wound. The attachment is made at any convenient point in the incision, there being less tension, as a rule, if the tube makes its exit through the middle of the incision.

6. Closure is effected in tiers. The peritoneal layer is closed by a continuous stitch of chromic No. 1 catgut (Fig. 4), and the anterior rectus sheath is closed with a series of silk mattress sutures, placed from a quarter to an eighth of an inch apart. This layer of sutures serves as a precaution against wound rupture and evisceration, an accident peculiarly likely to happen in aged and debilitated patients in whom the operation is frequently done. The skin is closed with Michel clips. The tube is clamped with a stopcock (Fig. 5) or a pair of forceps and is opened only when nourishment is introduced.

COMMENT

The Eiselsberg-Witzel technique, which has just been described, is a simple, quick method of creating a permanent, water-tight fistula for feeding purposes. The problem is not how to perform this operation, but whether to perform it and when to perform it. It is a procedure of desperation, as we have already intimated, and it should be resorted to only when no other surgery is possible. Its field, obviously, is very limited. Its usefulness is confined to those cases of gastric malignancy in which the lesion is obstructive and is so located or is of such an extent that the curative operation of gastrectomy or the more useful operation of gastro-enterostomy cannot be done. Balfour suggests, in addition, that jejunostomy be done in the occasional case in which there is some doubt as to the exact nature of the gastric lesion, and resection, for some reason, is impossible.

Benedict's suggestion in 1898 that jejunostomy should supersede both gastrostomy and gastro-enterostomy would find small approval today. There is still logic in his arguments, however, that a stomach invaded by a malignant process is not capable of sound digestion, and that a malignant lesion, even at the cardia, is likely to be further aggravated by the process of gastric digestion. Benedict's indications may be too liberal, but there is no doubt that the operation is sometimes justifiable, for in many cases the alternative is permitting the patient to starve to death before one's eyes. The choice is always a difficult one. Jejunostomy does nothing but delay the inevitable end, and sometimes does not delay it for long. It does, however, relieve pain, and it does eliminate the tortures of hunger and thirst, so that death comes in a kindlier fashion. For that reason it should probably be done more frequently than it is, and most certainly it should be done earlier than it is. Unfortunately, it is not usually given any consideration until the patient is exhausted from starvation and cachexia, and it is these factors, rather than the procedure itself, which are responsible for its high mortality.

Pre-operative preparation is not necessary. A patient about to starve to death should be operated on without delay. Postoperative care, aside from the usual measures which would be employed under any circumstances, consists chiefly of attention to the tube and care in the administration of nourishment. The tube should not usually be disturbed unless it becomes clogged or unless it slips out. In either of these contingencies it should be lubricated with some sterile oil or jelly before it is re-introduced. If the channel has been made sufficiently long, the opening in the bowel will be closed by *vis a tergo* when the tube is out, and leakage cannot occur. Re-introduction is easily accomplished by gradual, gentle pressure.

Water can be given in small quantities through the tube within an hour or two after operation, and feeding can be begun within 6 hours. The ideal diet should contain all the essential food elements, and should be at the same time bland, non-irritating, and easily digestible. Such a diet, as Wolfer points out, was devised by Ivy and his associates, and to them must go the credit for studying the subject of jejunal digestion in all its details and for devising a diet which is ample for nutrition, which preserves the water balance of the body, which prevents intestinal irritation, and which avoids deficiency states. Their formula includes milk, cream, sugar, flour, peptone, Ringer's solution and water, to which are added once a day, to supply the necessary vitamins, orange juice, egg, viosterol oil, Haliver oil, and yeast. It is also recommended that gastric juice obtained by aspiration of the stomach should be mixed with the pabulum.

The secret of success in jejunal feeding is the administration of the formula in small quantities at short, regular intervals, and at a rate which does not exceed the rate of the passage of the food from the stomach into the intestinal tract in the normal process of digestion. The amount of food should be increased very slowly, and intestinal cramps, diarrhea, nausea, or similar symptoms should be taken to indicate that too much food is being given at one time or that it is being given too rapidly.

We have found that the barrel of a Triumph syringe serves as a very satisfactory funnel for the introduction of the food (Fig. 5), and this method has the added advantage that the patient can feed himself as soon as he is able to sit up or move about. If the catheter has been introduced sufficiently far into the bowel, leakage or backflow of the food cannot occur, and if the jejunostomy channel has been made sufficiently long, digestion of the abdominal wall by the jejunal juices is an unlikely contingency.

These are the cardinal points in the operation of jejunostomy. It is a procedure of despair, but at least there is this to be said for it, that if it is done before the patient becomes too weak to endure any surgery, it is not in itself a lethal operation and it makes the final days of life more tolerable by freeing the patient from the suffering of hunger and thirst and pain. Furthermore, if the malignancy is of the slowly advancing type, and if the operation is done at an elective time, there is no reason why feeding cannot be continued almost indefinitely by this route, with a corresponding prolongation of life.

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REPAIR OF THE LIGAMENTS OF THE KNEE

Report of a New Operation for Repair of the Anterior Crucial Ligament

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RUPTURE or impairment of function of the crucial, mesial, and lateral ligaments is of rare occurrence when compared with injuries of the semilunar cartilages. Acute rupture of these ligaments is often united by conservative measures and undoubtedly there are instances of practically normal function in spite of non-union or elongation, which is an equation of individual compensation. However, continued disability with instability and evidence of slight derangement followed by acute symptoms from mild trauma, may be solely caused by permanent impairment of these structures. No knee is as efficient or as normal when there is deficiency of these ligaments and repair is indicated when there is only slight disability, especially in athletes and laborers, if it can be accomplished by a short and simple procedure.

English observers recognize injuries of the ligaments, and operative measures have been devised by Hey-Groves and others, for their repair, but, as expressed by Mr. Naughton Dunn and Mr. Rowley Bristow in their recent articles read in this country, they do not regard injury of these structures of much consequence. However, it is admitted that the excision of an offending cartilage does not give 100 per cent excellent results; the percentage in a large series of cases varies from 80 to 90 per cent. Some of the failures can be attributed to error in operative technique and traumatic arthritis induced by repeated injury to the joint from a detached cartilage, but there is undoubtedly a small percentage which present symptoms of sudden displacement or locking, not so severe as in a typical cartilage, but quite definite after the removal of a displaced cartilage. Occasionally normal semilunar cartilages are found at operation associated with undue laxity, or rupture of the crucial or lateral ligaments. Also, there is a small percentage which present symptoms of relaxed ligaments without definite signs of displacement or injuries of the cartilage. Exploration of such joints is often made with the removal of a "relaxed cartilage" or a fat pad, without relief.

However, when there is a rupture of a ligament or undue relaxation following partial rupture, there is in most instances displacement or fracture of one of the cartilages. Impairment of the anterior crucial and mesial ligaments is associated with injuries of the internal cartilage, while impairment of the posterior crucial and lateral ligaments is associated with injuries of the external semilunar cartilages.

In a survey of 183 cases of derangement of the knee-joint there were 30 in which there was sufficient evidence of ligamentous impairment to warrant operative procedures to repair these structures.

Only the anatomy of the lateral, mesial, and crucial ligaments of the knee-joint will be briefly reviewed.

The mesial or internal lateral ligament is attached above to the femur just below the adductor tubercle and below to the posterior portion of the inner aspect of the tibia to approximately 1½ inches below the joint line. This ligament is situated well posteriorly and is about 3½ inches long and from 1½ to 2 inches wide. It is intimately associated with the internal semilunar cartilage, and some of the fibers of the vastus internus are attached to the mesial surface.

The lateral or external ligament of the knee-joint is divided into two parts, the anterior or long ligament and the posterior or short ligament. The anterior rises above from the external condyle of the femur just anterior to the insertion of the external head of the gastrocnemius and is inserted below into the head of the fibula anterior to the styloid process. This ligament is a thick cord about 2 by 3 inches in length. The posterior or short ligament arises from the external condyle of the femur posterior to the long ligament and is inserted into the styloid process of the fibula. Both ligaments are separated from the joint by the popliteus tendon and are not in any manner associated with the external semilunar cartilage.

The location of the lateral ligament is parallel with the mesial ligament well on the posterior aspect of the joint; therefore, the mesial and the lateral ligaments in addition to the limiting lateral and mesial movement, limit extension of the knee-joint, and are thus on tension when the joint is fully extended. When a normal knee is fully extended, no motion to either side is possible as both ligaments are on tension.

The anterior crucial ligament is attached below into the upper surface of the tibia just anterior to

the spine of the tibia, and above into the posterior portion of the inner surface of the external condyle of the femur. There is an attachment to the external cartilage at the lower extremity of the ligament. The posterior crucial ligament is attached below to the upper surface of the tibia posterior to the spine and the posterior capsule, and passes upward, forward, and mesial to the anterior portion of the intercondylar notch, where it is attached to the anterior portion of the external surface of the internal condyle of the femur. A small ligament passes from the posterior portion backward to be attached to the external semilunar cartilage, which is known as the ligament of Wrisberg.

The anterior crucial ligament prevents hyperextension and is tense when the knee is fully extended. The posterior crucial ligament prevents backward displacement of the tibia when the knee is flexed and is tense in extreme flexion.

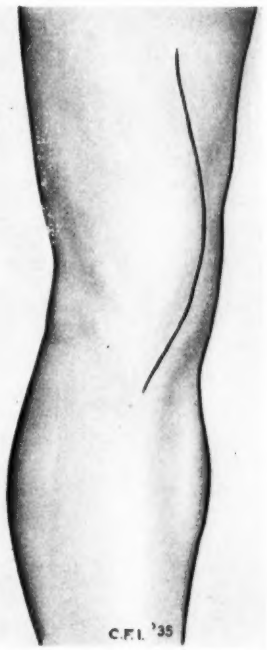

Fig. 1. Long medial incision giving access to anterior compartment of the knee-joint.

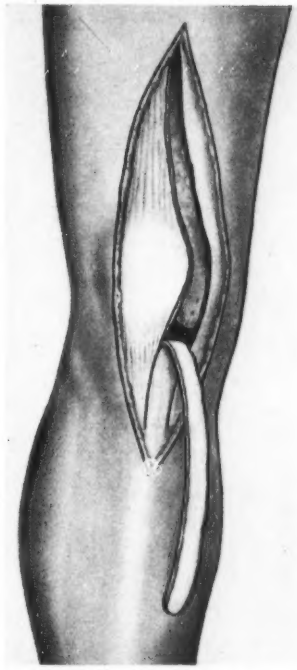

Fig. 2. Dissection of strip from tendon and capsule according to the description given.

The most frequent mechanism of injury to the mesial and anterior crucial ligament of the knee-joint is the same that causes injury to the internal semilunar cartilage, slight flexion with sudden abduction and external rotation of the knee. The most frequent mechanism of injury to the external or lateral ligaments and the external semilunar cartilage, are: forces in the reversed direction, slight flexion, adduction and internal rotation. Sudden hyperextension, as in the tackling of a leg from the anterior aspect in football, may cause hyperextension with injury or rupture to the anterior crucial ligament, or where the limb is fixed below the knee and the knee is hyperextended with the momentum of the weight of the body in action, as may occur by stepping into a post-hole. Rotation, twisting and shearing forces in the knee will rupture one or both crucial ligaments and also the mesial and lateral ligaments.

When there is a displacement of the internal cartilage, subsequent injuries can obviously injure the anterior crucial and the mesial ligaments, the latter being intimately associated with the internal cartilage. In fact, in all injuries of the internal cartilage there is almost always definite evidence of trauma to the internal lateral ligament, as denoted by tenderness over the attachments and often throughout the ligament.

The status of the mesial and lateral ligaments of the knee-joint is brought out in the routine examination with the knee fully extended, if the ankle is grasped with the right hand and the thigh fixed with the left. Lateral, rocking motion of the leg by the right hand will give excess motion externally if the internal or mesial ligament is ruptured or elongated; if the lateral ligament is ruptured or elongated, excess motion can be elicited internally. Examination of both knees should be made for comparison, as there are certain loose-jointed individuals in whom undue motion is present.

If the anterior crucial ligament is elongated or ruptured, the knee will glide forward on the tibia when flexed to a right angle, and to some extent in full extension when traction is made on the calf of the leg with both hands. Frequently the excursion will be as much as ¾ of an inch. In all cases of complete rupture this test is definitely

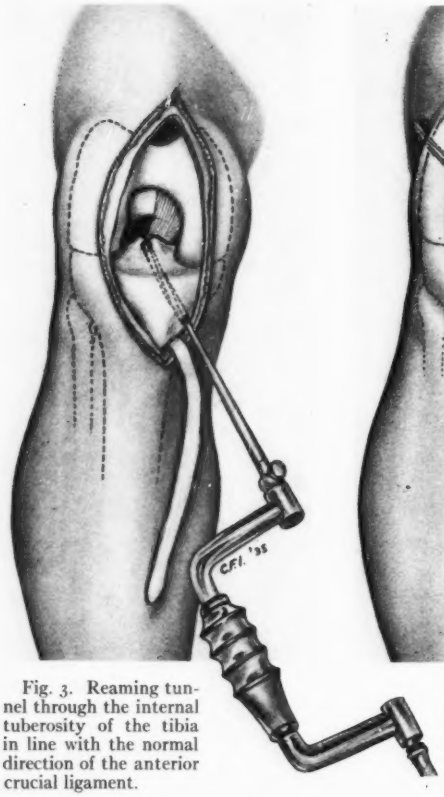

Fig. 3. Reaming tunnel through the internal tuberosity of the tibia in line with the normal direction of the anterior crucial ligament.

Fig. 4. Drilling tunnel in the external condyle of the femur in line with the direction of the anterior crucial ligament.

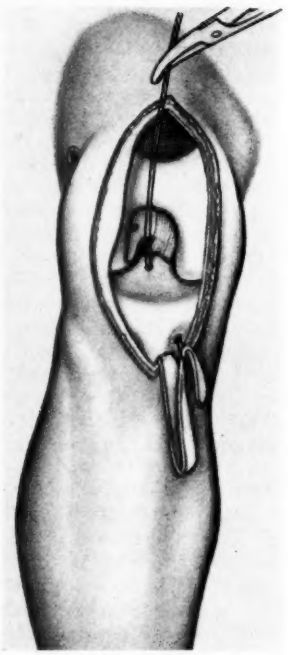

Fig. 5. Insertion of wire loop through tunnel in tibia, engaging end of strip.

positive. In impairment of the posterior crucial ligament the tibia will glide backward on the femur with the knee in flexion. When both ligaments are severed, as in complete dislocation of the knee-joint and after severe torsion force, the tibia can be made to glide backward and forward. However, in most injuries of this type there is usually so much reaction in the joint and extra-articular structures with formation of fibrous tissue, that there is rarely resulting instability and only conservative measures are necessary.

I have seen no instance in which the external or lateral ligament or the posterior crucial ligament was causing sufficient disability to warrant operative measures, though I do not doubt that there are instances in which such measures are required. The reason that the posterior crucial and lateral ligaments are rarely injured is that the mechanism which causes such injuries is of much less frequent occurrence, and also that the lateral ligaments are not connected so closely to the external semilunar cartilages as the mesial ligaments to the internal cartilage.

Further discussion will be confined to the operative technique for repair of the mesial and the anterior crucial ligaments. The technique for the repair of the mesial ligament was described in SURGERY, GYNECOLOGY AND OBSTETRICS, February, 1935,[1] and is as follows:

A skin incision is made parallel with the quadriceps tendon, the patella and patellar tendon, from 2 to 3 inches above the patella to just below the tibial tubercle. The deep fascia is incised and the capsule exposed. A curved incision parallel with the patella and the upper surface of the tibia is made into the knee-joint if internal impairment is suspected, and such attention given as may be required, after which the joint is closed. The repair of the ligaments is accomplished by dissecting from the inner aspect a strip of fascia lata, about 0.5 inch in width and 4 inches in length, from above down to a point about opposite the center of the inner aspect of the internal condyle of the femur. Two parallel incisions about 1 inch in length and about 1 inch apart are next made through the deep fascia and peri-

[1] Vol. 60, 214-5.

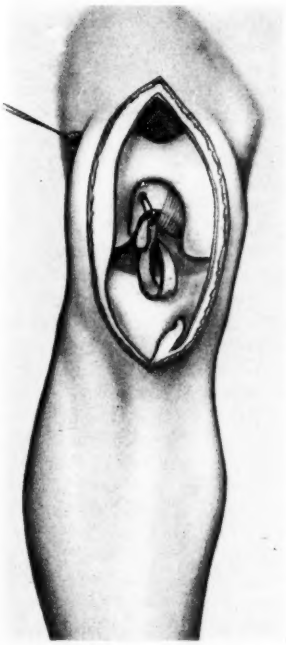

Fig. 6. New ligament drawn through tunnel in the tibia.

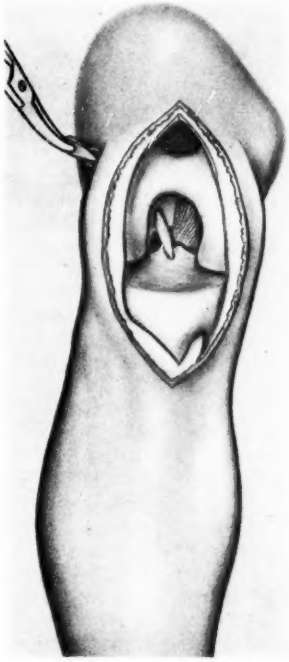

Fig. 7. New ligament drawn through tunnel in the external condyle of femur and made taut with the knee flexed about 150 degrees.

Fig. 8. Attachment of superior extension of the ligament to the periosteum and fascia lata.

osteum, about 1 inch below the upper extremity of the tibia and parallel with the joint line. If the tissue is not sufficiently firm, a tunnel may be made in the tibia at this point. An artery forceps is then passed through the lower incision close to the knee, emerging through the upper incision. The upper end of the fascial flap is grasped by the forceps and brought through the tunnel in the dense fascia and periosteum. After this the ligament is drawn tight and stitched as high as possible to the margin of the fascia lata from which it has been dissected. The limb is held extended and forcibly adducted during the operation. By passing the fascia through the tunnel a very accurate pulley action can be made, which permits effective tightening or tautness of the capsule.

Apparent impairment of the mesial and lateral ligaments is frequently observed after depressed fractures of the mesial and lateral tuberosities of the tibia. Such fractures do cause instability which is entirely due to loss in continuity of bone and not severance of the ligaments. Correction of this condition can be secured by a wedge-shaped osteotomy with the transplantation of bone on the depressed side after restoration of the anatomical alinement by elevating the tibial plateau to the normal plane.

Only rudiments of the crucial ligaments remain after complete rupture, therefore, a complete replacement must be made with other living tissues of suitable tensile strength. In the past we have always employed a pedunculated strip of fascia lata from the outer aspect of the same thigh to replace the anterior crucial ligament, as described by Hey-Groves. Following this procedure we have had very satisfactory results, but there was often too much local reaction, which made us think that possibly the procedure, often associated with removal of the internal cartilage, was too much surgery to one extremity. Therefore, the following operative technique was devised.

A longitudinal curved incision about 6 inches in length is made parallel with the quadriceps tendon, the patella, and the patellar tendon for complete exposure of the knee-joint. Dissection is made into the joint cavity throughout the entire incision and the interior of the joint inspected; the cartilage is excised if impaired. If the crucial ligament is severed, which can usually be determined on inspection, repair is made by dissecting

a long pedicle strip of fascia, capsule, and tendon from the lateral edge of the incision about ⅓ of an inch in diameter and 8 inches in length. It is dissected from above downward to the attachment of the capsule to the tibia. This strip contains very strong tendinous tissue from the medial border of the quadriceps and patellar tendons. A 6 millimeter drill hole is then made from a point on the anterior internal surface of the inner tuberosity of the tibia about 1½ inches below the joint, and emerges in the joint at the normal lower attachment of the anterior crucial ligament just anterior to the spine of the tibia. The same drill is then inserted into the intercondylar notch through the posterior portion of the external condyle of the femur, emerging under the skin above and posterior to the external condyle. A 3 inch incision is then made over the point of the drill with dissection down to the bone at this point. A rustless steel wire loop is then passed from above downward through the drill hole in each bone and the end of the pedunculated flap brought through to the superior exit of the tunnel in the external condyle of the femur. The flap is now drawn very taut with the knee in about 140 degrees flexion. About 3 inches of the strip should extend beyond the tunnel and is stitched to the periosteum and fascia lata. Both wounds are now closed in routine manner and a posterior splint applied with the knee in full extension, which further increases the tension on the new ligament. The ligament replaces anatomically the anterior crucial ligament, and there should be no undue anterior gliding of the tibia when the ligament is attached above. The operation requires only a few minutes and is attended with much less local reaction than other measures we have previously employed. The after-treatment consists in fixation by a posterior splint for a period of 3 weeks, when active and passive motion is instituted.

There were 30 cases, as above stated, which required repair of ligaments, 12 for rupture or evidence of laxity of the mesial ligament, and 18 for rupture of the anterior crucial ligament. In only 1 was the procedure carried out for undue laxity of the anterior crucial ligament.

The operation, as just described for the repair of the mesial ligament, was employed in 6 cases, 3 of which gave perfect results and in 3 it is too early to determine the end-result. Of the 5 in which older procedures were employed, 3 were excellent results, 1 complained of some pain and disability after 2 years, but was improved as compared with former condition. One could not be traced.

Of the 17 cases in which the anterior crucial ligament was ruptured, the operation described was used in 9 with apparent excellent results, but more time should elapse before conclusions can be reached. Of the 30 in whom ligaments were repaired, 9 were college football players and their education depended largely upon their return to the game. Seven of them were able to return the following season, from 6 to 10 months after operation, though they were apparently normal after 2 or 3 months. The result in 1 is too early to report. One case, a farmer, had a second injury with apparent rupture of the transplanted fascia lata about 6 months after operation, and is a probable failure. The others had excellent results. In 3 cases of rupture of the anterior crucial ligament in which the fascia lata was employed, a large hematoma occurred, which delayed healing but did not appear to affect the end-result. In 1, a superficial abscess appeared over the thigh where the fascia lata was removed, but healed promptly after drainage. Two cases observed immediately after injury are not considered in this series; in 1 case the ruptured anterior crucial ligament was sutured with excellent result, and in 1 the ruptured mesial ligament was sutured with excellent result.

The advantages of the procedures described are their extreme simplicity, minimum trauma, shorter incisions, and decrease in the time of operation, though excellent results may be secured by other methods herein mentioned.

The repair of these ligaments is more urgent in athletes and in those whose occupation requires strenuous labor. However, in a small proportion of all traumatic knees, possibly 10 per cent, restoration of ruptured ligaments will materially improve the end-results, especially if the procedures employed can be carried out rapidly and without undue intra-articular and extra-articular reaction.

EWING'S SARCOMA (ENDOTHELIAL MYELOMA)

Case Report with Necropsy

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MUCH has been done through the cooperative efforts of surgeons, pathologists, and roentgenologists in the past decade to clarify the many controversial issues in the field of tumors of bone. That much more work needs to be done is clear to anyone who has read the case reports and discussions concerning the clinical and pathological entity described by Ewing in 1927 under the name of "diffuse endothelioma of bone." Since that time fairly numerous case reports have appeared, most of them in the American literature, under various titles such as Ewing's tumor, Ewing's sarcoma, endotheliomyeloma, diffuse endothelioma of bone, undifferentiated round cell sarcoma of bone, etc. The diagnosis in most of these cases has been based upon skiagraphic evidence and microscopic examination of biopsy specimens or even upon clinical history and skiagrams alone. Relatively few of the cases have come to necropsy. Kolodny, in his monograph on bone sarcoma says: "As a general rule the patient is taken home before termination where he remains until death; necropsies of such patients are scarce." In 1933 Melnick found only five postmortem reports in the literature to which he added one. At least 4 more cases have been recorded in the literature during 1934, 1 by De Santo, and 3 by Connor. Even among these there are some which include insufficient detail and in one of them (Sycamore) the diagnosis was not supported by the histopathological findings. In an excellent critical review of the subject, Hirsch and Ryerson present convincing evidence to support the opinion that many published cases of so called Ewing's sarcoma are really bone metastases from primary carcinomas of the lung. Their analysis of the cases published as endothelioma of bone prior to 1922 shows that none of these can stand, on the basis of the data given, as unquestionable primary tumors of bone and in many cases the descriptions mark them almost certainly as metastatic carcinomas. Colville and Willis "strongly suspect that adrenal neuroblastomas will prove to be the primary growths in many of the cases."

In view of the varied histological picture presented by different cases of Ewing's sarcoma and the possibility of confusion with certain metastatic tumors, it seems wise to base generalizations with regard to this type of tumor upon data derived from cases that have come to necropsy. In such cases one can at least exclude nephrogenic neoplasms (hypernephromas), adrenal neuroblastomas, and bronchogenic carcinomas, provided the dissection has been carefully done and the findings recorded in sufficient detail. When the lungs contain large or extensive metastases it is not always possible to exclude beyond the shadow of a doubt the existence of a small bronchial carcinoma and a unilateral distribution is strongly suggestive evidence in its favor. In the case here described the equal symmetrical distribution of metastases, the uniformity of size of the tumors in the lungs, and the lack of demonstrable involvement of any of the bronchi argue strongly against this possibility.

CASE REPORT

No. 98641, Evanston Hospital. A married, white woman, aged 23, dress designer, was first seen at home on January 14, 1933. She was lying on her left side with both thighs flexed, complaining of severe pain in the right sacro-iliac region and in the right leg. The temperature was 100.4 degrees; pulse 110. A sensitive spot with some swell-

Fig. 1. Roentgenogram of pelvis made 10 weeks before death. The earliest involvement was in the left sacro-iliac region. Diffuse involvement of vertebræ, innominate bones, sacrum, and heads of both femurs is shown. The skull, ribs, clavicles, and sternum were also involved at this time.

Fig. 2. Sagittal section of upper thoracic spine (left); small piece of tumor from left innominate bone (upper right) with an irregular area of necrosis in its middle one-third; and surface view of rib (lower right) with periosteum removed to show metastatic tumors.

Fig. 3. Medial aspect of left lung. Tumor nodules are visible in the parenchyma of the lung and in the hilar lymph nodes on the left of the open incision and the extensive pleural involvement is shown on the right.

ing was found over the right sacro-iliac joint. The patient was unable to move on account of pain and with difficulty was turned on her back. She would not permit the thighs to be extended on account of the severe pain. She said that she had suffered three similar attacks during the past year but previously the pain had been on the left side. This was the first attack in which the right side was involved. An X-ray film, made October 31, 1932, was in the possession of the patient with the following report attached:

"Lumbosacral spine presented lateral curvature. Definition of sacro-iliacs was maintained but left presented some adjacent density increase and lipping of outer border at lower extremity, of possible osteoarthritic significance."

The patient stated that she had been under treatment for an acute arthritis of the sacro-iliac joint for several weeks. In order that a more thorough study of the case might be made and a definite diagnosis arrived at if possible, the patient was sent to the hospital on the next day.

On admission she had a temperature of 101 degrees; pulse 120; blood pressure 132–76. The following history was obtained:

She had been well until February, 1932, with the exception of infrequent colds and occasional attacks of tachycardia and palpitation. About a year ago she had fallen down stairs injuring her back, especially in the region of the coccyx, but at the time there was no external evidence of injury. In February, 1932, pain developed in the left sacro-iliac area, of moderate severity, accompanied by pain down the thigh. She received treatments by an osteopath and after 1 month the pain disappeared. There was no swelling and no disability, and the recovery was apparently complete. In the following July another similar attack occurred which was somewhat more severe and lasted about a week. Two months later (September, 1932) there was a severe attack during which the tissues in the region of the sacro-iliac joint became swollen and painful, with shooting pains down the leg and some weakness in walking. With this attack there was some elevation of temperature. Again the condition improved and the swelling seemed to disappear. In October the third attack began with great pain and swelling over the left sacro-iliac area, inability to walk, fever, sleeplessness, nausea, and numbness and pain down the back of the leg. This time the pain, swelling, and disability were persistent but the swelling on the left side had become less tender during the past month. During the last 2 weeks a similar attack had occurred on the right side with pain along the right sacro-iliac joint and in the lower part of the spine. This attack had been of the same character, accompanied by pain in the right leg, but was more severe than the attacks on the other side. She had lost 25 pounds during the past year.

At the time of admission to the hospital a distinct, hard swelling could be felt along the left sacro-iliac joint and a smaller but more sensitive swelling in the right sacro-iliac area. New X-ray films were made, with the following report by Dr. J. T. Case:

"It is very interesting that the films made October 31, 1932, showed apparently normal bone findings for the lumbar and pelvic regions and upper femora. At the present time we find after a period of fever, tenderness, hard swelling over the left sacro-iliac area, a marked condition of osteoporosis involving the left innominate bone, the head and upper end of the left femur and to a considerable extent the right innominate bone. The last lumbar vertebra

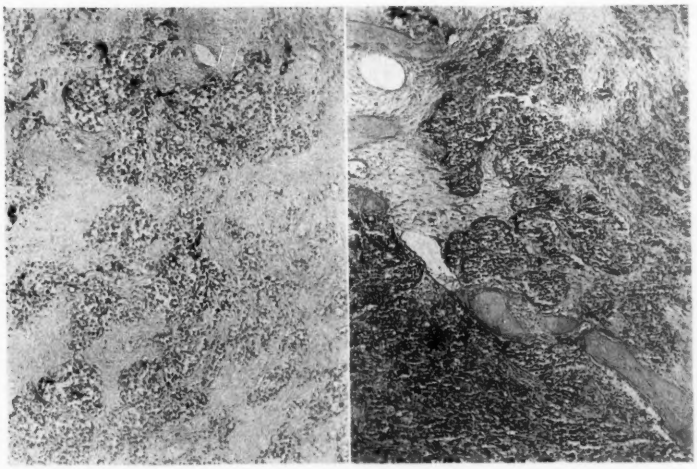

Fig. 4, left. Low power photomicrograph from fibrous portion of biopsy specimen. Strands and small islands of tumor cells are scattered through the dense fibrous mass. In this area the cells were small and uniform with clear cytoplasm and slightly resembling metastatic hypernephroma cells.

Fig. 5. Another area from the biopsy specimen showing lobulation of tumor cells and small trabeculæ of immature bone. In some places it was difficult to distinguish osteoblasts from tumor cells.

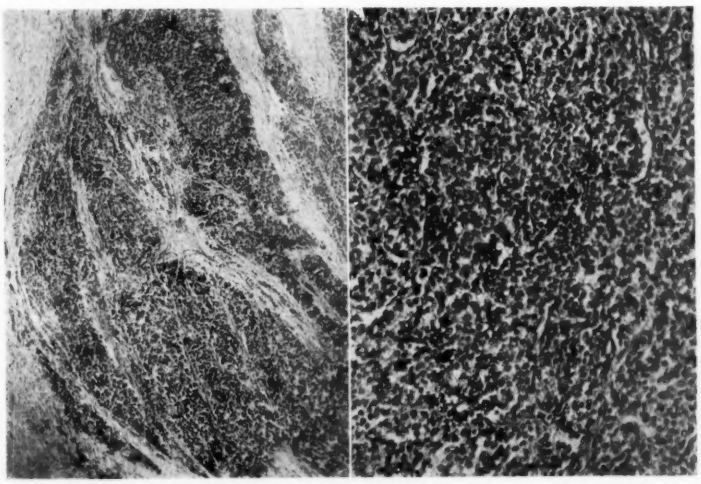

Fig. 6, left. Low power photomicrograph from the center of the tumor of the left ilium, adjacent to a large area of necrosis and fibrosis (on the left of the figure). The tumor cells are arranged in fascicles between slender fibrous strands.

Fig. 7. Higher magnification of section shown in Figure 6, showing the uniform size and structure of the cells. The small clear spaces between the cells are blood capillaries and (probably) lymph channels.

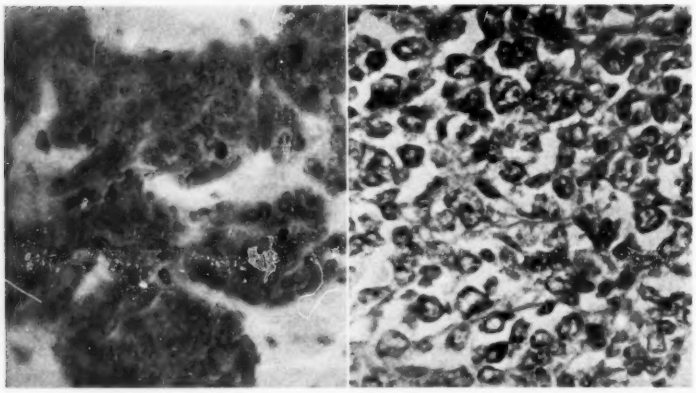

Fig. 8, left. High magnification of section from vertebra. The cells are less uniform than in the primary tumor, the arrangement compact and mitotic figures fairly numerous (four are visible in the figure).

Fig. 9. Section from the advancing margin of a metastatic tumor in the vertebral bone marrow. Here there is much more variation in size and shape of tumor cells than in any part of the primary tumor. A few bone marrow cells (dark nuclei in the picture) have been isolated in the mass of rapidly growing tumor cells.

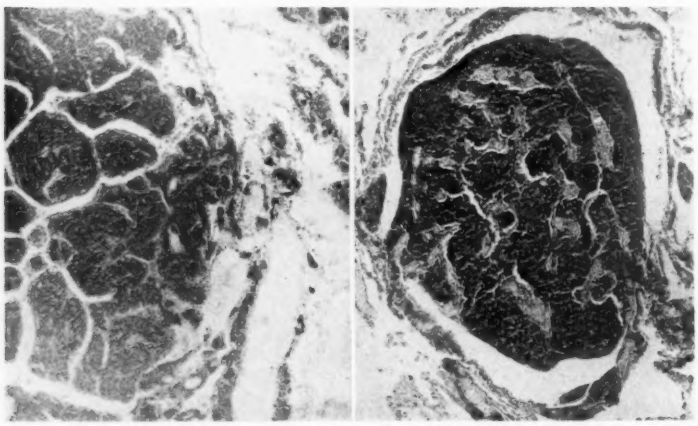

Fig. 10, left. Low power photomicrograph of lung illustrating lobulation produced by polypoid growth of tumor in alveoli. The perivascular lymph spaces also are filled with tumor cells.

Fig. 11. Polypoid mass of tumor tissue in a small bronchus. The tissue is richly supplied with blood capillaries.

seems to be sharing this process of osteoporosis. In the absence of any primary carcinoma, demonstrable, I would consider that this ought to be worked up from the standpoint of hyperparathyroidism."

The more important clinical laboratory findings at this time consisted of the following: Serum calcium, 8.8 milligrams; inorganic phosphates, 3.2 milligrams; Wassermann and Kahn, negative; urine showed no Bence-Jones protein. The sedimentation rate of the oxalated blood was 29.5 millimeters in 1 hour.

Although the clinical course and early X-ray examination, which showed changes in the sacro-iliac joint, were compatible with a diagnosis of osteomyelitis, the later film introduced another possibility. The clinical laboratory findings tended to exclude hyperparathyroidism. It was now felt that a biopsy was necessary, to differentiate the lesion further.

Accordingly, on January 18, 1933, an incision was made below the posterior part of the left iliac crest and along the sacro-iliac joint. Before the bone was reached a mass of

grayish, slightly vascular, dense tissue was found protruding into the muscle. A wedge of this tissue was removed. The cortex of the ilium was so fragile and soft that a probe could be pushed through it. With a curette a piece of bone from the ilium immediately beneath the protruding mass was removed. The incision was then closed. It is of interest that the biopsy wound closed and healed quickly by first intention and there was no sign of recurrence in the wound until just before the patient's death in the following June.

Extract from microscopic report: "Most of the tumor cells are pale, polyhedral with round or oval, pale nuclei only occasionally showing small, dark nucleoli. In the lobules the cells are packed close together without any intercellular substance, but some of the lobules are further subdivided into alveolar structures and cords by slender fibrous trabeculæ. In addition to the pale cells there are very small irregular masses and strands of hyperchromatic cells which do not have clear cell boundaries and the cytoplasm is so darkly stained that the nuclei cannot be clearly distinguished.[1] One section contains a few, scattered, atrophic, skeletal muscle fibers near the advancing margin of the tumor. Mitotic figures are moderately numerous in the more cellular areas (5 to 8 per high power field).

Tentative diagnosis: "Ewing's sarcoma."

Deep X-ray therapy was attempted but owing to the prostration which followed each treatment it was soon abandoned. For this reason no deductions could be made regarding the radiosensitivity of the tumor.

Subsequent X-ray examination of the skeleton showed progressive extension of the disease through the pelvis, into the lumbar spine, the hip joints, the upper ends of the femurs, the ribs, and skull (Fig. 1). No radiological examination was made of the small bones of the hands and feet or the long bones of the forearms and legs.

The later progress showed a number of interesting clinical developments. For instance, there were periods of a week or more when the temperature was normal or subnormal and then, apparently without reason, it would rise to 101 degrees or higher, showing fluctuations which suggested sepsis, receding daily for a week or 10 days and then returning to normal or a subnormal level. There were periods of several days, even as long as 2 weeks, during which there was evidence of general improvement with little or no pain and such a feeling of well being that the patient would talk about getting up. Not infrequently the period of improvement was followed immediately by severe collapse associated with dyspnea, restlessness, and great variations of the pulse. The following abstracts from the progress notes are of interest.

February 28, 1933. "X-rays show an extension of the malignancy with compression of the twelfth dorsal vertebra. For the first time, today she has had focal eye signs. The right eye is limited in all external movements: the patient is troubled with diplopia. A cerebral metastasis seems likely. Pulse remains very high."

March 10, 1933. "The eye signs mentioned in the last note cleared up completely after 4 or 5 days. She has failed steadily and in recent days has lost more weight, particularly noticeable in the face. Severe lancinating pain has been present for the last few days over the left scapula. The patient is clear mentally at times, but lapses into a state of irrationality or stupor. Her breathing during sleep particularly at night is at times Cheyne-Stokes in type with long periods of apnea. Fever has been absent for 2 days. Pulse is very weak but not as rapid as formerly. The patient certainly has few days to live."

She did live, however, almost 2 months. During this time the left eye became prominent (presumably due to a retrobulbar metastasis), three soft spots, each about the size of a quarter, appeared in the skull, and it was noticed that the size of the tumor in the region of the left hip was increasing very rapidly. A few weeks before death a collapse occurred, similar to the previous ones, with unconsciousness, respirations 8 per minute, pulse 48; the patient was thought to be dying. However, on the following morning the pulse had risen to 110, respirations to 20 and the patient was sufficiently alert to ask for her glasses and look over a magazine. Three weeks later, 1½ years after the first attack of pain, death occurred during a similar period of collapse. The mentality was clear up to the hour of death except while under the influence of morphine.

Necropsy. The necropsy was performed about 8 hours after death on the previously embalmed body. The examination was restricted to the trunk and consequently our knowledge of the degree of involvement of the long bones of the extremities and the bones of the skull is incomplete. An abstract of the necropsy record follows:

External examination of the body revealed extreme wasting of the soft tissues, flexion deformity of the hip and knee joints and a partly healed decubitus ulcer over the sacrum. The biopsy wound was perfectly healed and the scar was stretched over the surface of a firm, dome-shaped tumor, measuring about 8 by 5.5 by 2 centimeters which protruded from the lateral aspect of the left ilium. The scalp was thin and the tumors in the calvarium could be easily outlined by palpation. A firm node, 2 centimeters in diameter, protruded from the surface of the left parietal bone about 2 centimeters from the median line; another of about the same size in the right parietal bone, 1 centimeter from the midline; three on the right side and one on the left of the occipital bone, measuring up to 2.5 centimeters in diameter and elevated 2 to 4 millimeters above the surface of the bone. No tumors could be demonstrated by external examination of the long bones of the extremities, although their surfaces could be outlined readily by palpation. The breasts were small and free from tumor masses. There was moderate edema of the feet and ankles.

When the chest wall was uncovered, numerous firm nodules, 1 to 2.5 centimeters in diameter were seen protruding from the outer surfaces of the first to the sixth ribs, inclusive, on the right side, the first to the seventh ribs, inclusive, on the left side and from the medial end of the left clavicle. The tumors were much more prominent and more numerous when viewed from the inner aspect of the chest wall. All of the ribs were found to be involved and one showed sixteen separate nodules and fusiform enlargements on its inner surface. One large nodule was attached to the inner and superior aspect of the sixth costal cartilage. When the ribs were split, the tumors were found to be embedded in the cancellous portion, the larger masses having destroyed the cortex, elevated the periosteum and in a few places the periosteum had been penetrated and the fascia and muscle invaded.

Several tumor nodules from 5 to 10 millimeters in diameter projected from the posterior surface of the middle one-third of the sternum. Similar nodules in large number, many of them confluent, protruded from the lateral and anterior surfaces of the thoracic vertebræ. So much of the bone had been destroyed in the bodies of the upper thoracic vertebræ that slices could be removed with a sharp knife and no red marrow could be distinguished on surfaces made by section (Fig. 2). The tumor tissue here was similar to that in the ribs and sternum and consisted of a fairly firm, gray to grayish-yellow, homogeneous substance with-

[1] An artefact due to crushing.

out gross evidence of retrogressive changes. No protuberances were found on the surfaces of the lumbar vertebræ but on section, several poorly defined masses measuring up to 2 centimeters in diameter were found embedded in the cancellous bone of each vertebral body.

A large, smooth tumor attached to the inner aspect of the left ilium and sacrum, involving practically the entire left wall of the pelvis, encroached upon the pelvic organs from the left side. The periosteum was apparently intact over its entire surface. Several yellow areas of necrosis were found on sections made through the middle of the main tumor. Small spicules of bone were encountered in various portions of the tumor but chiefly at its periphery. The crest and anterior portion of the ilium were firm but all portions contained masses of tumor tissue. The cortex of the right ilium was apparently unbroken though reduced in thickness in many places and the cancellous portion was largely occupied by yellow-gray tumor tissue.

Visceral metastases. Grossly visible metastases were confined to the lungs and thoracic lymph nodes. The pleural surfaces of the lungs were studded with small and large protuberant nodes which were discrete in the apical portions and in a narrow zone along the hilus of each lung, but elsewhere they were confluent and covered practically the entire surface (Fig. 3). In the lung parenchyma the nodes were for the most part discrete and measured up to 18 millimeters in diameter. They were scattered fairly evenly throughout both lungs and replaced approximately one-half of the parenchyma of each. The intervening lung parenchyma was compressed by the tumors and contained a slight excess of fluid. The peribronchial lymph nodes were firm, solidly filled with yellow-gray tumor tissue and measured up to 1 centimeter in diameter. The tracheobronchial and paratracheal nodes were enlarged up to 3 by 2 by 1 centimeters and their parenchyma was almost entirely replaced by firm, homogeneous tumor tissue. The lining of the trachea, primary and secondary bronchi was smooth and pale. (The smaller bronchi were examined by cutting the previously hardened lungs into thin slices. Many were compressed by tumor nodules.) Thick cords of tumor tissue, parallel to the blood vessels and bronchi, and probably representing dilated lymph channels, were found in all portions of both lungs.

The thyroid and parathyroid glands were grossly normal. No glandular tissue could be seen in the extremely thin pad of fat which represented the thymus gland. The epicardial fat was thin and gelatinous. The myocardium was red brown and the mitral valve showed slight fibroplastic deformity. The liver was small (about 1 kilogram). No tumor nodules could be found in its substance. The gall bladder and bile ducts were normal. No gross alterations could be found in the stomach, intestine, pancreas, suprarenal glands, kidneys, ureters, urinary bladder, uterus and adnexa, spleen, abdominal lymph nodes, and blood vessels.

Histopathology. All tissues for section were fixed in formol-Zenker solution and sections of the tumor were stained with Giemsa, Van Gieson, and Mallory (connective tissue) stains in addition to the routine hematoxylin and eosin.

Bones (ilium, vertebral bodies, and ribs). The tumor is composed of polyhedral cells with oval nuclei and scanty, unstained cytoplasm. The nuclei contain fine chromatin nets, coarse and fine granules, and a few have acidophilic nucleoli (Figs. 4, 7, and 8). The cell boundaries are practically indistinguishable in those areas in which the cells are compact but in some places fine cytoplasmic processes can be seen joining one cell to another. The masses of compactly arranged cells are traversed by coarse septa of connective tissue and divided into small, irregular lobules by a network of fine strands of fibrous tissue resembling the form of an irregular honey comb (Figs. 5, 6, and 7). Within the small lobules, no intercellular substance is present. The fibrous framework contains numerous fine blood capillaries and a few empty spaces resembling lymph channels (Fig. 7). Small, isolated fragments of degenerated bone are scattered through the tumor tissue and slender trabeculæ of newly formed osteoid tissue are found in some of the thick fibrous septa, especially in sections taken from the periphery of the pelvic tumor where remnants of the displaced periosteum can be recognized. In a few places, thick, anastomosing trabeculæ of newly formed bone and osteoid tissue are embedded in cellular portions of the tumor at some distance from the periosteum (Fig. 5). In these no lamellar structure is present. Small marrow spaces containing reticular tissue and tumor cells are found in the larger trabeculæ. The margins of the trabeculæ are lined by cells resembling osteoblasts, arranged irregularly and in many layers. Most of these are considerably smaller than the cells of the neoplasm. Some parts of the tumor fail to show any lobular arrangement. In these the cells are especially compact and most of them are spindle-shaped. Sections of the pelvic tumor mass (left ilium) contain large areas of coagulation necrosis with actively growing tumor tissue at the periphery (Fig. 6). In the lumbar vertebral bodies the marrow cells are generally hyperplastic with cells of the granulocytic type (myelocytes and myeloblasts) in marked preponderance. The marrow cells are especially numerous and compact at the advancing margins of masses of tumor cells. A considerable number of lymphoid cells and cells resembling plasma cells are mixed with the granulocytes in the hyperplastic zones. There is no indication in the sections that these are derived from the tumor cells.

Noteworthy variation in size of the tumor cells is observed in the region of these advancing margins of secondary tumors (vertebræ and ribs, Fig. 9) in contrast to the uniformity of size in the main tumor mass and especially in the biopsy sections (compare Figs. 4, 6, 7, and 8).

Visceral metastases. Lung. In the metastatic nodules, the lobular arrangement is similar to that found in the bone tumors. The larger nodules have replaced the lung parenchyma so that the alveolar walls and bronchioles have been entirely obliterated; but in some areas the dilated alveolar spaces and small bronchi have been filled in by polypoid masses of tumor cells and their vascular stroma, resulting in a peculiar, sharp lobulation in which each lobule represents an alveolar space (Figs. 10 and 11). Small tumor masses are found in the perivascular and peribronchial lymph channels, and in some places they appear to lie free in the air sacs. In the central portions of the largest nodules the stroma is increased to such an extent that small clumps and strands of tumor cells are isolated in the poorly cellular stroma. The cells of this stroma are small spindle shaped cells resembling fibroblasts.

Peribronchial lymph nodes. The finely lobular structure of the tumor masses is similar to that found elsewhere and there is a suggestion of alveolar arrangement with most of the nuclei located at the periphery of the lobule and relatively abundant faintly eosinophilic cytoplasm. Interlobular mucoid stroma is abundant in the central part of some of the nodes.

Suprarenal glands. Several small solid masses of tumor cells, some of them in the form of emboli within sinusoids, are found in both cortex and medulla. The cortical structure appears normal and the medulla contains abundant chromaffine tissue.

In the kidneys there is evidence of subacute glomerulonephritis, but there were no metastatic tumors in the sections. Both liver and spleen contained an abnormally large amount of hematogenous pigment. Pancreas was normal.

SUMMARY AND DISCUSSION

In summarizing the clinical features of the case, it should be noted that all of the features which have been emphasized as characteristic of this disease were present: from the history of trauma to bone in a young individual, followed by symptoms suggesting osteomyelitis with fever, swelling and pain, recovery in a few weeks, attacks recurring at shortening intervals, becoming more severe and finally persisting in some one bone. Finally the patient died with tumors in the skull, extremities, spine, ribs, lungs, and lymph nodes, 1½ years after the appearance of the first symptoms. (Variations in duration of life from 5 months to 16 years were noted by Kolodny in the Registry material.) The skeleton in this case was so extensively involved and the process so diffuse at the time of the second X-ray examination that an osteoporosis due to hyperparathyroidism was suggested.

The tendency to widespread diffuse involvement is characteristic of the disease but may be closely imitated by other tumors both primary and metastatic. During the same year in which this case was under observation we had opportunity to examine a case of multiple myeloma (myelocytic type) which had showed a strikingly similar roentgenographic picture in the pelvis, ribs, and spine. Connor found most difficulty in differentiating metastatic lymphomatous tumors from Ewing's sarcoma.

Following diagnosis by biopsy, X-ray therapy was instituted but was soon discontinued on account of the severe prostration which followed each treatment and the rapid spread of the tumor was apparently unaltered by it. In some of the earlier publications, the prompt response of Ewing's sarcoma to adequate radiotherapy was emphasized. In Connor's opinion this is an erroneous conclusion. He believes that in this respect it is much like malignant endotheliomas arising in other tissues and that in radiosensitivity it stands midway between osteogenic sarcoma and highly sensitive tumors such as metastatic lymphosarcoma and neuroblastoma in bone. A combination of irradiation and surgery has been found to give the best results in treatment according to Geschickter and Copeland "yielding about 10 per cent of permanent cures."

The effect of biopsy upon the tendency of the tumor to metastasize is a problem which has been much discussed but is still far from final settlement. Geschickter and Copeland are of the opinion that "exploration does not necessarily affect the prognosis in cases in which radical operation or X-ray treatment follows exploration." This is supported by the data recorded by Crowell from the Registry of Bone Sarcoma. Of the 9 cases of Ewing's sarcoma with clinical cures of 5 years or more, all were subjected to surgery, 6 were treated by amputation and of the amputation cases 4 cases had 1 or more surgical procedures at some period prior to the amputation. Opposed to this view there are many who advise strongly against any incision of the tumor and advise radiotherapy to the tumor on the basis of clinical and roentgenologic diagnosis. It must be confessed that had we proceeded on such evidence in this case, the procedure adopted would have been either an exploratory operation in the neck or radiotherapy to the region of the parathyroid glands. The difficulties and failures in diagnosis from biopsy specimens have been fully discussed by Kolodny and many others in case reports and reviews of this subject.

Further discussion at this time of the question of histogenesis of Ewing's sarcoma seems futile in view of the scanty evidence presented in the published cases and with such striking variations between individual cases. The microscopic evidence in this case seems to favor no particular theory. While the formation of new bone was a conspicuous feature in the tumors of the skeleton, there is no direct evidence that the tumor cells themselves were responsible for the laying down of new bone. No bone formation occurred in the metastases of the lungs or other soft tissues except the muscle outside of the main tumor where there was abundant opportunity for the displacement of hyperplastic osteoblasts along with the disruption of the periosteum. The formation of vascular channels within the intra-alveolar and intrabronchial, polypoid tumors of the lung is not conclusive evidence of angioblastic properties since it is just as reasonable to assume that the vessels of the alveolar walls were appropriated by the tumor cells as they formed the protrusions into the alveolar and bronchial lumina. Furthermore, similar pictures have been observed in other metastatic tumors of the lung where no question of endothelial origin could be raised. Likewise, hyperplasia of the cells of the bone marrow at the borders of spreading foci of tumor cells is frequently seen in metastatic carcinoma, in the early stages before fibrosis has appeared, and in itself is no proof that the hyperplastic blood cells are derived from tumor cells. No myeloid cells, either immature or mature, were associated with the tumors in the lungs or lymph nodes.

The general biological characteristics such as diffuse growth and widespread involvement of the skeleton suggest a relation to multiple myeloma but pulmonary metastases seem to contradict this relationship. Connor's view, that the cell of origin

is an undifferentiated mesenchymal cell (reticulo-endothelial cell?) which may become differentiated "into adult reticulo-endothelium, into the hemohistioblast, or into endothelium," which may lay down cement substance and become an angio-endothelioma or which, under other circumstances, may become an osteoblast, is very attractive and serves to bring together the various theories of origin but requires much more proof before the question can be finally settled.

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REGIONAL ENTERITIS (NON-SPECIFIC)

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NON-SPECIFIC inflammatory tumors of the gastro-intestinal tract have been reported at various times in the medical literature but they have been considered medical curiosities rather than well established clinical entities. In 1932 Crohn, Ginzburg, and Oppenheimer separated from this group an inflammatory lesion of the terminal ileum which they believed to be a clinical and pathological entity. In their first report, these authors described a lesion which, in their series of 14 cases, was limited to the terminal ileum. Shortly after their report Harris, Bell, and Brunn reported a case with an inflammatory lesion of the jejunum pathologically identical with the lesion described by Crohn and his co-workers. Subsequently, there have appeared in the medical literature rather numerous reports of cases with a chronic non-specific inflammation of ileum, jejunum, and colon. Recently Crohn added to his first report 3 cases in which the chronic non-specific inflammatory process he described for the ileum was found in the jejunum and upper ileum. He also reports a condition in which the inflammation of the terminal ileum is associated with an inflammation of one or more segments of colon. The segments of colon appear fiery red and are covered with exudate, but are separated by wide areas of normal colon. It appears that this regional inflammation of the jejunum, ileum, and colon is indistinguishable pathologically from the lesion of the terminal ileum originally described by Crohn and his co-workers. Although indistinguishable pathologically, the lesions at different levels of the intestinal tract, on account of their location may give rise to different symptoms. Regional enteritis of the terminal ileum, the regional ileitis described by Crohn, may present a clinical picture which differs from the regional enteritis of the jejunum or colon. The symptoms likewise vary according to whether the inflammatory process is acute or chronic or whether it is associated with ulceration or stenosis, or both, of the intestine.

During the past 2 years we have had 8 cases of regional enteritis. In 1 case the inflammatory process was in the lower jejunum, and in the 7 remaining cases the lesion was in the terminal ileum. Four of the patients with lesions of the ileum had an acute regional enteritis, 2 had a chronic regional enteritis with stenosis, and 1 had a chronic regional enteritis with an external fistula.

The pathological anatomy of regional enteritis is that of a non-specific inflammation with excessive connective tissue reaction. Although the pathological process is continuous and progressive, it can be divided for clinical purposes into three stages: (1) acute regional enteritis, (2) chronic hypertrophic enteritis with stenosis of lumen, and (3) chronic enteritis complicated by external or internal intestinal fistula.

Acute regional enteritis of the terminal ileum in our series occurred in 4 cases. In these patients, as seen at operation, the peritoneal cavity contained a small amount of serous fluid. The terminal 15 to 30 centimeters of the ileum was edematous and hyperemic in 2 patients and in the 2 remaining, congested, purplish-red, soggy, and enlarged to about one and one-half times its normal size. The process stopped abruptly at the ileocecal valve. On the proximal side it disappeared gradually in 2 cases and stopped abruptly in 2. The ileal peritoneum was smooth and glistening. The regional mesenteric lymph glands were hyperplastic. In the 3 cases that underwent spontaneous resolution the mesentery, although hypermic at operation, was not thickened or edematous. In the case that failed to resolve spontaneously, the mesentery of the ileum was edematous, although the involvement of the ileum grossly appeared about the same as in the cases that did resolve spontaneously. It may be that the absence of thickening and edema of the mesentery, indicates that the inflammatory process is still limited to the ileum and perforation of the ulcerative process into the mesentery has not occurred; whereas, the association of a thickened edematous mesentery with a regional enteritis may be indicative of a perforation into the mesentery with abscess formation. This tendency toward perforation into the mesentery is more pronounced in the cases of chronic regional enteritis. Spontaneous resolution, once perforation into the mesentery has occurred, is probably less likely to take place than if the process is limited to the bowel wall. The state of the mesentery of the involved ileum may be, therefore, an indication as to the treatment to be followed, i.e. whether to resect, shortcircuit, or leave alone.

Since most cases of acute regional enteritis are treated conservatively, there has been little opportunity to study the changes in the mucosa and the muscular layer of the diseased bowel. Jackman, Erb, and Farmer report cases of inflammation of the terminal ileum, the description and illustrations of which correspond closely to the macroscopic appearance of the ileum in one of our patients in whom diagnosis at operation was acute regional enteritis and who recovered spontaneously. In Jackman's cases, "The mucosa over a wide area had been replaced by a firm hemorrhagic exudate with roughened surface. The transition between the disease and healthy segment was somewhat abrupt. The mucosa was more severely ulcerated along the mesenteric side of the bowel. Microscopic examination revealed a condition of simple intestinal ulceration. The mucosa throughout the affected area had been completely destroyed and replaced by a thick fibrinopurulent exudate. In the bowel wall generally there was an acute inflammatory reaction lessening in degree toward the subperitoneal layer which showed congestion, edema, and interstitial hemorrhages, but few polymorphonuclear cells. This was in marked contrast to the condition in the submucosa and muscle layers where in places the degree of polymorphonuclear cell infiltration approached abscess formation. Evidence of previous acute inflammation of the bowel was present in the form of much dense scar tissue."

The pathological changes in the chronic forms of regional enteritis have been thoroughly studied, since these are the lesions most frequently resected (Figs. 1, 2, 3, 4). When seen at operation the peritoneal cavity contains a small amount of serous fluid. The inflammatory process in the ileum either stops abruptly at the ileocecal valve or continues into the cecum, and extends orally for about 15 to 35 centimeters, gradually shading off into normal intestine. The mesentery of the involved bowel may be 2 centimeters thick. Fistulas are often found between the terminal ileum and adjacent bowel, usually the sigmoid. Walled-off abscesses in mesentery are not rare.

Examination of resected specimens shows the wall of the ileum thickened, as a result of inflammatory hyperplasia of all the layers. This hyperplasia is greatest near the ileocecal valve where the wall may reach three to four times the normal thickness. The mucosa is swollen, the intestinal folds thickened. Along the mesenteric border of the mucosa there are linear ulcerated areas a few millimeters in diameter. In the region of the ileocecal valve, there are areas of papillary and polypoid hyperplasia. The lumen of the ileum is usually constricted, and the narrowing most pronounced in the region of the ileocecal valve. The ulcerations along the mesenteric border in all our ileal specimens showed a tendency toward perforation. This was illustrated by roentgenograms of the specimens taken after distending the ileal lumen with a solution of barium sulphate (Figs. 5, 6, and 7). The earliest perforations were in the form of linear fistulas that began in mucosal ulcers along the attachment of the mesentery and penetrated the bowel wall to the region of the subserosa. As the ulceration progressed, the sinuses penetrated through the bowel wall and led into a common cavity in the mesentery, which at operation was found to be an abscess.

During the perforation of these sinuses a neighboring loop of bowel, usually colon, as occurred in Case 5, becomes adherent to the ileum and a fistula becomes established between them. A second mechanism whereby internal fistulas develop is ulceration of a mesenteric abscess into an adherent loop of bowel. The abscesses in the mesentery, although usually small, often become large enough to simulate an appendiceal abscess. When these abscesses are drained a persistent fistulous tract may become established between the ileum and the abdominal wall.

The cecum when involved becomes constricted at its distal end by a hyperplastic inflammatory process which appears to extend from the ileum and invade the cecal wall. The thickening of the cecal wall is greatest at the ileocecal valve and gradually diminishes distally into normal cecum and ascending colon. The mucosa of the cecum in our cases showed no ulceration.

Histologically, the chronic forms of regional enteritis show no changes to indicate one of the recognized granulomas, such as syphilis, tuberculosis, actinomycosis, or Hodgkin's disease. The mucous membrane of the ileum in our specimens was irregularly ulcerated (Fig. 8). The ulcers were lined by a non-specific granulation tissue which was extensively infiltrated by polymorphonuclear leucocytes. A chronic non-specific granulation tissue extended diffusely, throughout the muscular layer and into the subserosa. This granulation tissue contained nodular granulomas which were composed of histocytes and fibroblasts, with an occasional foreign body giant cell and a peripheral zone of lymphocytes (Figs. 9 and 10). In some sections these giant cells contained vegetable fibers. The presence of foreign body giant cells, as suggested by Moschowitz and Wilensky, undoubtedly has led many observers to make a diagnosis of hyperplastic ileocecal tuberculosis in cases of chronic regional ileitis.

The pathological process in our patient with regional enteritis of the jejunum consisted of a stenosis of the lumen of the jejunum with ulceration and perforation at the site of stenosis. The perforation was walled-off by fibrinous exudate and adherent small bowel. The jejunum proximal to the lesion was distended, its wall edematous, hyperemic, and somewhat like the ileum in acute terminal ileitis although not so thick. A microscopic section from the site of obstruction showed a marked infiltration of the bowel wall by a non-specific inflammatory granulation tissue.

Regional enteritis may occur in individuals of all ages. Rockey reports a case of thickening of the terminal ileum, apparently an acute regional ileitis, in a child aged 5; and Brown, Bargen, and Weber report a case in a man aged 61. It occurs most commonly, however, in young adults. The youngest of our series was 7 years and the oldest, 34 years of age. The incidence as to sex was 3 females and 4 males. Crohn, Ginzburg, and Oppenheimer and Brown, Bargen, and Weber found the ratio of males to females was about 2 to 1.

The symptoms of regional enteritis according to the classification of Crohn and his co-workers may be divided into four groups: (1) signs of "acute surgical abdomen," (2) symptoms of ulcerative colitis, (3) symptoms of chronic obstruction of the small intestine, and (4) persistent and intractable intestinal fistulas that follow drainage of an abdominal abscess.

The symptoms in 4 patients of our series simulated those of an acute appendicitis. Abdominal pain was the outstanding symptom. At the onset, the pain was diffuse and colic-like. Cramps occurred in paroxysms with relative freedom from symptoms between paroxysms. The child aged 7 years in our series, while being examined, had abdominal cramps which doubled him up and caused him to cry. The pain lasted 1 to 2 minutes and then subsided for about 4 to 5 minutes, when it recurred. This colic-like intermittent pain which resembled the pain of an acute intestinal obstruction was present in 3 cases of acute regional enteritis of the ileum that were confirmed at operation. There was no history of diarrhea in any case. The fever in these acute types varied from 99 to 101 degrees F. A moderate polymorphonuclear leucocytosis was present.

Abdominal examination showed tenderness in the right lower quadrant. General physical examination was otherwise negative. This association of the symptoms and physical signs of an acute appendicitis with those of an acute but incomplete intestinal obstruction is very suggestive of an acute regional ileitis.

The symptoms of the chronic form in which the inflammatory process in the ileum has produced a stenosis of the intestinal lumen, are those of a low grade small intestinal obstruction. For a period of months to a year, as occurred in our group, the patients complain of abdominal cramps, particularly after indiscretions in diet. Mild abdominal distention is present. The general symptoms and signs of sepsis, such as loss of weight, anorexia, moderate anemia, persistent low grade fever, and leucocytosis are usually present. One of our patients, besides these symptoms, had repeated attacks of severe right lower quadrant pain associated with a fever of 102 to 103 degrees F. and right-sided tenderness. These symptoms would last for about 2 days and then subside. At operation she had a mesenteric abscess which was walled-off by small bowel. The paroxysms of pain and fever were probably due to the gradual extension of the abscess and localized peritonitis.

Physical examination of the abdomen of patients with the stenotic form of regional enteritis of the terminal ileum discloses mild distention and a mass in the right lower quadrant. The mass is most frequently felt abdominally although in one of our cases the mass lay to the right of the uterus and was felt only on pelvic examination.

The patient in our series who had progressed to the fistulous stage gave a history of drainage of an abdominal abscess. Subsequently, a sinus persisted and resisted all forms of medical treatment. Recovery followed resection of the diseased bowel and fistulous tract.

Although Crohn and his co-workers report the frequent occurrence of diarrhea and symptoms simulating an ulcerative colitis, only 1 of our patients gave a history of diarrhea and none noted gross blood in the stools.

The symptoms in our case of regional enteritis of the jejunum were those of an intestinal obstruction of gradual onset. Within 3 weeks of the onset the patient developed symptoms of an acute intestinal obstruction with feculent vomiting, abdominal distention, visible peristalsis and obstipation.

Roentgen-ray examination of the gastro-intestinal tract of cases with regional enteritis of the terminal ileum is entirely negative, or shows a filling defect in the terminal ileum. Barium enema usually fails to show any changes in the colon. The head of the cecum in some cases is narrowed, especially in the region of the ileocecal valve. If the ileocecal valve is incompetent, a filling defect in the terminal ileum is noted. A barium meal usually gives more definite findings.

When our cases of acute regional enteritis that subsided spontaneously were examined roentgenologically 1 month after operation the terminal ileum showed only the rapid intermittent passage of barium through it. Three months after operation the involved ileum appeared normal. The case of acute regional enteritis of the ileum that progressed to the chronic form developed a filling defect just proximal to the ileocecal valve. In the fully developed chronic stenotic forms, barium meal usually shows a filling defect in the terminal ileum with a mild ileal stasis and distention proximal to the defect. If the constriction is limited to the last few centimeters of the ileum, and only partially occludes the bowel, the filling defect may be overlooked. In the chronic cases in which the inflammatory process involves a longer loop of ileum, the involved loop appears as a narrow rigid tube in which valvulæ conniventes are not seen (Figs. 11 and 12). In the more advanced cases with still greater stenosis, the involved loop's lumen roentgenologically resembles a cotton string. Kantor calls this the "string sign," analogous to the "string sign" described by Crane in the spastic colon.

Fistulous communication between the ileum and colon may lead to delayed motility or to a mild constriction at the site of the fistula. Careful roentgen examination with a barium enema may disclose a fistula between the colon and terminal ileum. Injection of an opaque medium, such as iodized oil, into an external fistula which results from a regional enteritis should show the connection between the fistula and the small intestine, usually terminal ileum.

The treatment of the acute types of regional enteritis depends upon the stage of the inflammatory process. If the inflammation is limited to the terminal ileum and the mesentery is uninvolved, resection may not be necessary, since the process may resolve spontaneously. If, however, the mesentery is thickened, indurated, and edematous, the ulceration of the ileum may have extended into the mesentery. In these cases, spontaneous resolution is less likely to occur, so that a short circuiting operation or a resection of the involved bowel is the better procedure.

In 3 cases of acute regional enteritis, the terminal ileum alone was involved without an associated edema or thickening of the mesentery. All these cases resolved spontaneously. Rockey, Erb, and Farmer report similar cases of spontaneous recovery in children in whom the terminal ileum was edematous and injected. In 1 patient of ours the mesentery of the involved ileum was thickened and edematous. Believing that the process would go on to spontaneous resolution, we did an appendectomy to simplify subsequent diagnosis and closed the abdomen. The patient's symptoms recurred 3 weeks later and became progressively more severe. A resection of ileum, cecum and ascending colon was done. This operation was followed by recovery.

The treatment of the chronic stenotic forms of regional enteritis consists of either shortcircuiting the intestinal contents around the lesion, i.e. ileocolostomy to the transverse colon, or of resecting the diseased bowel. If a resection is done, a long loop (20 to 30 centimeters) of normal bowel adjoining the lesion should be removed also so as not to leave behind any small focus of inflammation which might be overlooked on gross examination. Postoperatively, such a small overlooked focus may progress and lead to a fresh stenosis of the bowel. This complication occurred in several cases reported in the literature. In our cases, resection of the involved bowel with a wide margin of normal intestine on either side of the lesion has given excellent results. Shortcircuiting operations reported by Brown, Bargen, and Weber, Clute, and others have given relief in about 50 per cent of the patients. In the other 50 per cent the pathological process progressed so that a resection of the involved bowel became necessary. Since shortcircuiting operations are associated with less risk than a resection, it may be that a two stage resection for cases of regional enteritis is the procedure of choice. If the symptoms disappear following the shortcircuiting, no further surgery is indicated. If, however, the symptoms persist or become progressively worse, resection becomes necessary.

Regional enteritis complicated by persistent external intestinal fistula can be cured only by excision of the involved intestine and sinus tract. Attempted closure without resection usually fails. Crohn reports a case in which eight laparotomies were performed in a vain attempt to close an intestinal fistula following drainage of a right lower quadrant abscess. As soon as the pathological process was recognized to be a regional ileitis, the involved intestine was resected with the fistulous tract. Complete relief of symptoms and cure of the fistula followed.

CASE 1. T. F., aged 7 years, was first examined September 17, 1933. The child was apparently well 3 days before examination. After eating several hamburger sandwiches which had caused him no distress, his mother gave him a "prophylactic dose" of castor oil. The next day the child complained of diffuse abdominal pain and nausea. The pain became intermittent, cramp-like, and localized to the lower abdomen. The following day the pain became more

Fig. 1. The involved ileum appears as a stiff tube. The serosa is dull, in places granular, and subserosal hemorrhages are present.

severe and colic-like. The cramps caused the patient to double up and cry. The paroxysms of pain lasted for about 1 minute and subsided, following which he was comfortable. Upon admission to the hospital, the cramp-like pain recurred about every 4 to 5 minutes. Vomiting occurred several times since the onset.

Fig. 3. This resected specimen shows the wall of the terminal ileum thickened, the hyperplasia greatest at the ileocecal valve. The head of the cecum is hyperplastic. The mesentery of the ileum is thickened and contains a small abscess, which was walled-off by the adherent loop of ileum that is seen covered with fibrinous exudate in the proximal end of the resected specimen. The lumen of the terminal ileum is narrowed; the narrowing is greatest at the ileocecal valve.

Fig. 2. Specimen in Figure 1 cut open longitudinally. Note hyperplasia of the wall of the ileum, edema of the villous folds, and ulceration along the mesenteric side.

Physical examination revealed a well nourished male child of about 7 years. The temperature was 100 degrees F; pulse rate 98; and respiratory rate 18. Abdominal examination revealed tenderness in the right lower quadrant. No masses were palpated. Rectal examination showed no masses or pelvic tenderness. The remaining physical examination was negative. The white blood count was 12,000. A provisional diagnosis was made of an acute appendicitis.

At operation the appendix was found to be grossly normal, the terminal 10 centimeters of ileum was thickened and indurated, the serosa was injected. The regional lymph glands were enlarged up to 3 centimeters and several were hemorrhagic. The ileum proximal to the diseased portion was normal and not dilated. A diagnosis was made of acute regional ileitis. Believing that the pathological process would resolve spontaneously, an appendectomy was done to simplify subsequent diagnosis and the abdomen closed.

Following the operation the gastro-intestinal tract was examined roentgenologically every 2 to 4 months. At first

Fig. 4. This specimen shows a more advanced stage of regional ileitis. There is marked hyperplasia of the wall of the terminal ileum. The wall of the cecum is thickened, particularly in the region of the ileocecal valve. The mesentery contains many sinuses which lead into the lumen of the terminal ileum. The mucosa of the terminal ileum is granular and contains sessile and pedunculated polyps. Proximally, the mucosa is edematous, the villous folds are blunted and thickened. The lumen of the terminal ileum is constricted and almost obliterated at the ileocecal valve.

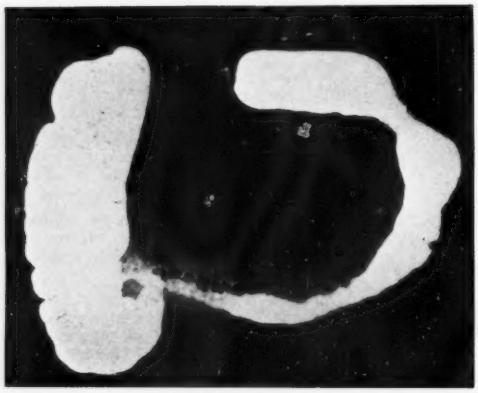

Fig. 5. Roentgenogram of specimen in Figure 1, inlected with a watery solution of barium sulphate. The jumen of the ileum is uniformly narrowed. The constriction is more pronounced at the ileocecal valve and gradually diminishes proximally. In the distal portion of the ileum there are many sinuses which seem to have penetrated all the coats of the bowel wall to the subserosa. The cecum appears normal.

the last portion of the ileum was spastic so that it retained little or no barium for a distance of 10 to 12 centimeters. Subsequently, the spasm was released and peristaltic waves could be seen traversing the entire involved ileum into the cecum. The last examination was on December 2, 1934, at which time the entire gastro-intestinal tract was normal. The patient had had no recurrence of his pain.

Case 2. Mrs. M. P., aged 21, was admitted to the Cook County Hospital on October 8, 1933. She complained that 16 hours before admission she noted the gradual onset of diffuse abdominal pain which at first was constant, dull, aching in character. Besides this constant distress the patient had periodic attacks of lower abdominal colic-like pain, which would last for from 1 to 2 minutes and then gradually subside. The patient described these pains as similar to labor pains, although less severe. Nausea was present, but no vomiting occurred. There was no history of any previous similar attacks. The remaining general history was essentially negative.

Physical examination revealed a poorly nourished adult white female, 21 years of age who appeared acutely ill. During the examination the patient would frequently double up when the colic-like pain appeared; but after it had subsided, she was relatively comfortable. The temperature was 101 degrees F.; pulse rate 100; respiratory rate, 18. Abdominal examination showed tenderness in the right lower quadrant. No mass was palpated. The remaining physical examination revealed nothing of apparent importance. The white blood count was 10,000. The urine was normal.

Since the symptomology in this case was strikingly similar to that of Case 1, a diagnosis was made of a regional ileitis. However, an acute appendicitis could not be excluded. The patient was operated upon immediately. The appendix was grossly normal. The terminal 16 centimeters of the ileum was edematous and thickened. The ileum proximal to this area appeared normal. The regional lymph glands were enlarged. A diagnosis of acute regional ileitis was made. The appendix was removed to facilitate subsequent diagnosis and the abdomen was closed. The patient made an uneventful recovery. She was last seen November 4, 1933, at which time she was free from distress and roentgen examination of her gastro-intestinal tract revealed a normal terminal ileum.

Case 3. Mr. T. R., aged 34, colored, was admitted to the Cook County Hospital July 26, 1934. He complained of general abdominal pain, fever, nausea and vomiting for about 39 hours. He was well until July 24, 1934 when at 2 o'clock in the morning he was awakened with a diffuse abdominal pain which was more intense in the right lower quadrant. The pain was colic-like and radiated toward the right costal margin and at times to the left lower quadrant. The colics recurred every 3 to 4 minutes. The patient took a dose of magnesium sulphate which he immediately vomited. The pain increased in severity. Shortly after the onset he had a watery bowel movement but none since then. He had never had a previous similar attack. The remaining history disclosed nothing of apparent importance.

Physical examination revealed a fairly well nourished colored male aged 34 years. He had a temperature of 102 degrees F.; pulse rate, 110; and respiratory rate, 24. His abdomen was tender, throughout, but most tender in the right lower quadrant. The peristaltic sounds were normal. There were no masses. The general physical examination was otherwise negative. He had a leucocytosis of 10,250.

A diagnosis was made of acute appendicitis. However, at operation the appendix was grossly normal. The last 25 centimeters of the ileum was purplish-red, edematous, and about one and one-half times its normal size. The wall of the ileum was thickened and soggy. The lumen was narrowed. The involvement of the bowel was more pronounced at the ileocecal valve, diminished proximally, and disappeared about 25 centimeters from the ileocecal valve. The mesentery of the involved ileum was injected, but not thickened. The regional lymph glands were not enlarged. The cecum and ascending colon appeared normal. The small bowel elsewhere appeared normal. An operative diagnosis was made of an acute regional enteritis of the terminal ileum. On account of the possibility of the spontaneous resolution of the inflammation of the ileum, an appendectomy was done to facilitate subsequent diagnosis, and the abdomen was closed.

The immediate postoperative course was uneventful, but approximately 12 hours after the operation had been performed the patient's temperature rose to 104 degrees F.; pulse, 140; and respiratory rate, 44. His skin was covered with a cold perspiration. He remained in this condition for about 36 hours. He was given large quantities of saline solution by hypodermoclysis, but failed to improve. On the beginning of the third postoperative day he was given saline solution intravenously. Shortly after this his condition began to improve. About 3 weeks after operation the patient developed a pain in the right chest which persisted about a week and subsided. X-ray of the chest showed a thickening of the pleura in the region of the right lower lobe and a moderate amount of fluid on the same side. There was no evidence of pulmonary tuberculosis. Subsequent roentgenograms of the chest showed the pathological process in the right base to be subsiding. Roentgen examination of the colon with a barium enema showed a normal colon. The ileocecal valve was competent. Examination of the terminal ileum following a barium meal showed a normal terminal ileum. The patient was last seen March 10, 1935. He had had no recurrence of his abdominal distress and had gained about 10 pounds in weight.

Fig. 6. Roentgenogram of specimen in Figure 3 shows the barium filled sinuses penetrating through the wall of the ileum and leading into a common cavity which, at operation, was found to be mesenteric abscess.

CASE 4.[1] Mr. H. A., aged 20, first consulted us on January 4, 1933. For 2½ years he had had recurrent attacks of diffuse abdominal colic-like pain. This pain was sharp, paroxysmal, and seemed to be aggravated by eating. There was no nausea, vomiting, or diarrhea. Shortly after the onset of this illness he consulted a physician under whose treatment (non-residue diet and mineral oil) the symptoms disappeared for a year. The pain then recurred. It was more severe and tended to localize to the right lower quadrant. The pain remained colic-like in character; the colics lasted about 3 to 5 minutes and then tapered off to a dull constant ache or disappeared completely. The abdomen became somewhat distended. There was no melena or diarrhea. The patient lost about 20 pounds in weight during the last 2½ years. His history otherwise contained nothing of apparent importance.

Physical examination revealed a poorly nourished white male who did not appear acutely ill. The temperature was 98 degrees F., pulse rate, 90; and respiratory rate, 20. Examination of the abdomen showed a moderate distention. The peristaltic sounds were increased, but no peristaltic waves were seen. A firm mass about 6 centimeters in diameter was palpated in the right lower quadrant. The mass seemed immobile but was not tender. The liver and spleen were not enlarged. Physical examination was otherwise negative.

The erythrocyte count was 4,968,000; leucocyte count, 19,600; and hemoglobin, 80 per cent. The blood Kahn and Wassermann reactions were negative.

Roentgen examination of the gastro-intestinal tract showed an annular "napkin-ring" filling defect of the terminal ileum (Fig. 14). Proximal to this constriction, the ileum was dilated. The remaining gastro-intestinal tract was roentgenologically normal. The diagnosis made was "obstructive lesion of the terminal ileum."

The patient was operated on January 6, 1933. The abdominal cavity contained a small amount of serous fluid. The terminal ileum was enlarged to about one and one-half times its normal diameter. It showed a hard edema. The serosa was dull and covered by fibrinous exudate. The process extended proximally from the ileocecal valve for about 25 centimeters and then gradually shaded off into normal ileum. About 10 centimeters from the ileocecal valve there was an internal fistula between the diseased ileum and the middle of the transverse colon. The mesentery of the terminal ileum was somewhat edematous. The

[1] Cases 4 and 5 were previously reported in the Surg. Clin. of N. Am., 1935, 15: 697.

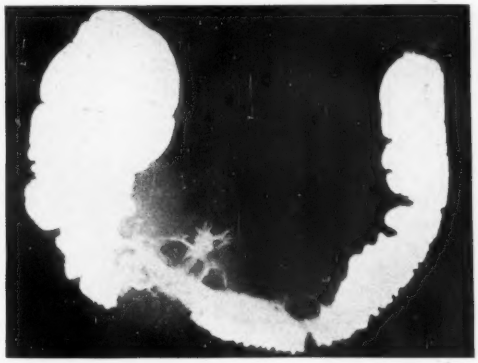

Fig. 7. Roentgenogram of the specimen in Figure 4. There is a filling defect in the terminal ileum. The lumen of the last portion of the ileum is narrowed. The constriction is most marked at the ileocecal valve. Along the mesenteric attachment there are five sinuses which extend from the lumen of the involved ileum into the mesentery where they meet in a common cavity from which barium seems to diffuse farther out in the mesentery. Along the antimesenteric border, the filling defect of the ileum is irregular and mottled. This appearance is caused by the inflammatory polyps in this region. Proximally there is a second constricted area along the mesenteric side of which two sinuses penetrate from the lumen into the mesentery. The cecum is narrowed but its contour is smooth and regular.

regional mesenteric lymph glands were enlarged. The lesion appeared similar to the "terminal ileitis" described by Crohn and his co-workers. We closed the opening in the transverse colon and resected about 35 centimeters of the colon and restored the continuity of the bowel by uniting the ileum to the transverse colon with a lateral anastomosis. Following the operation he was given a transfusion of 500 cubic centimeters of whole blood. The subsequent postoperative course was uneventful.

The patient was examined last in January, 1935. He had gained about 40 pounds in weight and had experienced no recurrence of his abdominal distress. Roentgen examination showed a normal colon, well functioning ileocolostomy and a normal ileum.

Pathological report. The resected specimen consisted of the terminal 35 centimeters of the ileum, with cecum, appendix and ascending colon (Figs. 1 and 2). The terminal 20 centimeters of the ileum was thickened and resembled a rubber hose in consistency. On the serosa covering this portion of ileum there was some fibrinous exudate. About 15 centimeters from the ileocecal valve along the mesenteric border of the ileum, there was a fistula which communicated with the lumen. When opened, the lumen of the entire involved ileum was seen to be narrowed, the narrowing becoming more marked toward the ileocecal valve. The bowel wall was thickened, measuring about 5 millimeters. The lesion involved all the layers. The mucosa was edematous, and along its mesenteric border there were many longitudinal ulcerations that in places seemed to extend through to the subserosa. Roentgen examination of the specimen distended with a watery solution of barium sulphate (Fig. 4) showed the narrowing more pronounced at the ileocecal valve and tapering off proximally. In the terminal portion of the ileum there were many small sinuses which extended

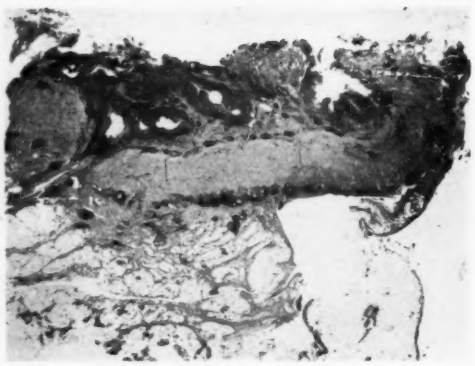

Fig. 8. There is hyperplasia of the wall of the ileum, most marked in the muscularis and subserosa. The mucosa is extensively ulcerated.

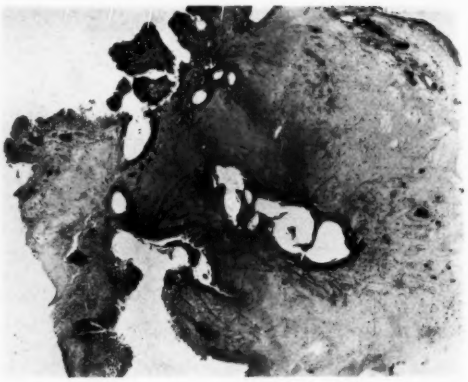

Fig. 9. Photomicrograph from specimen in Figure 3. Ulceration in terminal ileum extends through bowel wall into mesentery where it enters an abscess cavity.

from the mucosa toward the mesentery. Some of them seemed to penetrate through the muscularis to the subserosa. The cecum appeared normal.

Histological sections showed the wall of the ileum much thickened, partly by hypertrophy of the muscular layer and partly by an extensive inflammatory process that involved the submucosa and, to a greater degree, the muscularis and subserosa (Fig. 8). This inflammatory infiltration consisted of nodular granulomas composed of hyaline connective tissue with many fibrocytes, histocytes and occasional giant cells (Fig. 10). The granulomas were surrounded by accumulations of lymphocytes. The giant cells were of the foreign body type. In places, they seem to surround vegetable fibers (Fig. 11). The mucosa was occasionally ulcerated. The base of the ulcers was formed by recent subacute inflammatory tissue.

CASE 5.[1] Mrs. L. B., aged 32, was seen by us June 18, 1934. She complained of cramp-like lower abdominal pain for about 7 weeks. Her history was that 2½ months previously she delivered a full term child. About 2 weeks following delivery she noted the gradual onset of cramp-like lower abdominal pains. The cramps would last up to 2 minutes and then subside. She consulted her obstetrician who discovered that she had a temperature of 99 to 100 degrees F. daily, and a tender mass in the right tubo-ovarian region. On account of the recent childbirth and the above findings, a diagnosis of a puerperal infection was made. The patient was hospitalized and placed at bed rest for 3 weeks. The abdominal cramps and fever persisted. She left the hospital and remained in bed at home for several weeks with no relief of her symptoms. The general history contained nothing of importance relative to her abdominal complaints.

Physical examination revealed the abdomen somewhat distended. Visible peristalsis was noted, particularly in the lower abdomen. There were no areas of tenderness and no masses were palpated abdominally. Pelvic examination disclosed an orange-size, tender, fixed mass in the right fornix. The uterus was normal in size and position. The left fornix appeared normal. The remaining general physical examination revealed nothing of apparent importance. The erythrocyte count was 4,640,000; leucocyte count, 8,700; and hemoglobin, 95 per cent. Differential blood count showed neutrophils 82 per cent; lymphocytes, 12 per cent; eosinophils 2 per cent; and monocytes, 4 per cent.

Roentgen examination of the colon showed a filling defect in the head of the cecum. Barium regurgitated into the ileum but the outline of the terminal ileum could not be seen clearly on account of the overlying sigmoid. Examination of the ileocecal region after a barium meal disclosed a narrowing of the last 12 centimeters of ileum. Proximal to this constriction the bowel was slightly dilated (Fig. 13). The head of the cecum showed the same filling defect noted with the barium enema. The stomach and remaining small bowel were normal. On account of the history of a low grade fever for 2 months with symptoms of partial intestinal obstruction due to an obstructive lesion of the terminal ileum, a diagnosis of regional enteritis of the terminal ileum was made and resection advised.

The patient was operated upon June 21, 1934. There was a small amount of serous fluid in the peritoneal cavity. In the right fornix the mass that was previously palpated was a tumor involving the terminal ileum and the cecum. The pelvic organs were normal. The mass was not attached to the surrounding structures and was easily delivered from the abdomen. The last 15 centimeters of ileum was thickened, edematous, and hose-like. The serosa was covered with fibrin and was hyperemic. The mesentry of the involved ileum was thickened and edematous. A resection was done of the last 25 centimeters of the ileum, the cecum and ascending colon. An ileocolostomy to the transverse colon was done with a lateral anastomosis After operation she was given a transfusion of 500 centimeters of whole blood. The remaining postoperative course was uneventful. She last was seen May 1, 1935. At that time she was free from abdominal distress and had gained weight. Barium enema showed a well functioning ileocolostomy and a normal ileum.

Pathological report. The resected specimen (Fig. 3) consisted of 26 centimeters of ileum with the attached cecum and colon. The distal 7 centimeters of ileum was surrounded by a mass having a maximum diameter of 8 centimeters. The serosa covering this portion of ileum was covered with fibrin. The appendix which was incorporated in this mass was surrounded by fibrous tissue so as to form a cylindrical structure measuring 3 centimeters in diameter and located on the posterior surface. Upon section, the tumor mass around the ileum was seen to be composed

[1] Cases 4 and 5 were previously reported in the Surg. Clin. of N. Am., 1935, 15: 697.

Fig. 10. An area in the subserosa shows infiltration by a non-specific granulation tissue, which is surrounded by lymphocytes and lateral to it lies a foreign body giant cell.

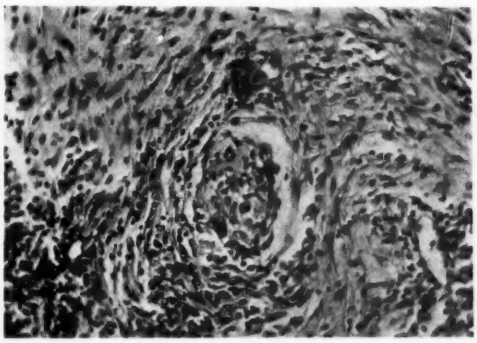

Fig. 11. A higher magnification of a granuloma shows several giant cells which surround areas containing vegetable fibers.

of fibrous tissue within which were islands of fatty tissue. The lumen of the bowel was narrowed to 3 millimeters in the narrowest diameter, and 8 millimeters in the widest portion. The mucosa was granular and projecting from its surface were several pedunculated polypoid masses measuring up to 1 centimeter in length. The entire cecum was shrunken, its wall thickened, the mucosa roughly granular, injected, but not ulcerated. The thickening of the cecal wall was chiefly due to an increase in the submucosa. This thickening gradually diminished in passing to the ascending colon, which was grossly normal. The mesentery of the ileum was greatly thickened and indurated, increasing to 4 centimeters at the ileocecal valve. Within the mesentery, sinus tracts were easily followed into the lumen of the ileum, and connected with one another. The proximal ileum exhibited a moderate thickening of the muscular coat (hypertrophy) with dilatation of the lumen to as much as 3.5 centimeters in diameter. The histological findings in this case were the same as in Case 4.

Injection of the specimen with barium sulphate (Fig. 7) showed a filling defect of the cecum which corresponded essentially to the filling defect seen in the roentgenogram before operation. The terminal ileum was narrowed. Along the mesenteric border, 5 sinus tracts were followed from the lumen into the mesentery where they converged to a central irregular mass of barium (abscess cavity). Proximally, in the ileum there was a second narrow portion at which point two small sinus tracts extended from the bowel into the mesentery. There was a filling defect on the antimesenteric surface in this area. The remaining ileum and colon appeared normal in contour.

Case 6. Mrs. F. P., aged 25, was referred to us by Dr. Charles Pugh, on June 1, 1934. She complained that 2 days prior to admission she noted the gradual onset of a bloating and abdominal distention. She had no desire for food. About 24 hours after the onset she experienced a sudden sharp pain in the right lower quadrant of the abdomen. The pain lasted about 5 minutes and was later followed by continuous pain in this region. The sharp colic-like pain occurred about every hour and was severe enough to awaken her from sleep. There was no nausea or vomiting. The remaining history disclosed nothing of apparent importance.

Physical examination at the time of admission to the hospital showed the patient fairly well nourished and not acutely ill. She had a temperature of 100 degrees F.; pulse rate, 90; respiratory rate, 18. Examination of the abdomen disclosed tenderness in the right lower quadrant. No other abnormal signs were noted. The general physical examination was essentially negative. The white blood count was 11,000. On account of the indefinite abdominal pain and tenderness localized over the appendix, with a leucocytosis, a diagnosis of acute appendicitis was made. The patient was operated upon immediately. The ileum was found enlarged to about one and one-half times its normal size; its walls were edematous and soggy. The mesentery of the involved ileum was thickened to about 1.5 centimeters. The cecum and appendix appeared normal. The pathological process grossly was that of a regional enteritis of the terminal ileum. On account of the possibility of spontaneous resolution, we removed the appendix to facilitate subsequent diagnosis, and closed the abdomen. The postoperative course was uneventful. She was discharged from the hospital on the tenth postoperative day. Shortly after the patient was home she developed a dull, continuous pain in the right lower quadrant with paroxysms of abdominal cramps. About 1 month after operation she developed recurrent paroxysms of severe pain in the right lower quadrant associated with a temperature of 103 degrees F. The pain and fever lasted for about 13 hours and gradually subsided. These acute attacks occurred about every 4 to 7 days. No nausea or vomiting was noted. There was no diarrhea or melena. The patient gradually lost weight. Roentgen examination of the ileocecal region following a barium meal on two occasions during the postoperative period showed transitory spasm of the terminal 4 to 6 centimeters of the ileum. No constant filling defect was demonstrated. The ileum proximal to the spastic portion was slightly dilated. Barium enema showed no pathology in the colon. The cecum showed slight narrowing in the region of the ileocecal valve. Barium regurgitated into the ileum which in its last 2 centimeters showed a filling defect, whereas, the bowel proximal to this point appeared normal. On account of the recurrent pain and fever, and the filling defect in the terminal ileum, a diagnosis was made of a stenotic type of regional enteritis.

The patient was re-operated upon on July 5, 1934. There was a small amount of serous fluid in the peritoneal cavity. The disease in the terminal ileum was more extensive than at the first operation. A loop of ileum was adherent by fibrinous exudate to the mesentery of the terminal ileum. Upon separating this loop of ileum from the mesentery, a small abscess cavity was opened. The last two feet of the ileum, cecum, and ascending colon were resected and a side-

Fig. 12. A barium enema shows the cecum uniformly constricted in the region of the ileocecal valve. The remaining colon is normal.

to-side anastomosis was done between the ileum and transverse colon. After operation she was given a transfusion of 500 cubic centimeters of whole blood. The remaining postoperative course was uneventful. She was last seen May, 1935, at which time she had gained 10 pounds in weight and her abdominal symptoms had disappeared.

Pathological report. "The specimen (Fig. 4) consists of 50 centimeters of the ileum with the cecum and ascending colon. The mesentery at the ileocecal angle is thickened to about 3 centimeters and appears as a firm mass, 8 by 8 centimeters partially encircling the bowel. Within this mass there is an abscess 1 centimeter in diameter. In the proximal portion of the resected ileum the bowel is surrounded by fibrinous exudate which forms one of the walls of the above mentioned mesenteric abscess. The lumen of the distal 2 centimeters of ileum is narrowed to 6 millimeters in diameter; elsewhere the lumen is of normal size. The wall of the terminal 8 centimeters of the ileum is thickened to 5 millimeters. The hyperplasia involves all the layers. The mucosa is edematous and the villous folds are thickened. Linear ulcers of the mucosa are present along the mesenteric attachment of the last 5 centimeters of the ileum. The wall of the cecum in the region of the ileocecal valve is thickened to 6 millimeters. The mucosa in this portion of ileum is edematous, but contains no ulcers."

The microscopic findings were essentially similar to those described in Case 4. A section taken through the ileum including the ileocecal valve (Fig. 9) showed ulceration of the mucosa penetrating through the bowel wall and leading into an abscess cavity in the mesentery.

Injection of the specimen with barium sulphate showed a filling defect in the terminal ileum involving the ileocecal valve (Fig. 4). On the mesenteric side of the filling defect, small sinus tracts are seen extending out from the bowel into the mesentery where they coalesce into a large irregular mass of barium which corresponds to the walled-off mesenteric abscess noted during the operation.

CASE 7. Mrs. C. U., aged 27 years, was first examined September 22, 1930. For the past 3 years she had recurrent attacks of cramp-like periumbilical pain which occurred during and after meals. The pain was often associated with diarrhea. There was no nausea or vomiting. Her last attack began 1 week prior to our first examination at which time she experienced severe paroxysmal lower abdominal cramp-like pain which was accompanied by vomiting. No diarrhea was present with this attack. There was no vomiting until the last attack. The past history relative to the present illness was that when aged 11 years the patient had an abdominal complaint which continued for about 1 year. The pain at that time was periumbilical and occurred during and after meals. She was free from distress until 18 years of age when an appendectomy was performed for this indefinite abdominal distress. Following the operation she remained well until the onset of her present illness 3 years ago.

Physical examination revealed a poorly nourished adult white female who did not appear acutely ill. The temperature was 98 degrees F.; pulse rate, 80; respiratory rate, 16. Abdominal examination showed an appendectomy scar, diffuse lower abdominal tenderness and slight distention. No masses were found on abdominal palpation, but pelvic examination revealed a tumor mass in the right adnexal region. The remaining physical examination was negative. The diagnosis made was a pelvic tumor.

The patient was operated September 23, 1930. The small intestines in the lower abdomen and pelvis were matted together by fibrinous adhesions. While separating the loops of bowel, an abscess was opened into. Several drains were placed into the abscess cavity and the abdomen closed without further exploration. Subsequent to the operation the patient developed a fecal fistula which persisted up to the time she was discharged from the hospital October 27, 1930.

The patient remained under observation for about a year, during which time the fistula resisted all types of non-surgical treatment. On account of the failure to close, resection of the fistula was advised.

At operation the fistulous tract led to the terminal portion of the ileum, which was thickened and edematous. The last 20 centimeters of ileum was resected, and the continuity of the gut restored by a lateral anastomosis between the ileum and the cecum. The patient made an uneventful recovery. She was last seen November 5, 1934, when she was free from abdominal complaint.

We regret that the specimen and histological sections of this case have been lost. However, at the time of operation, the resected bowel was found thickened and the mucosa was ulcerated along the mesenteric border. The appearance macroscopically was that of a regional ileitis.

CASE 8. Mrs. C. P., aged 31 years, was admitted to the Cook County Hospital October 17, 1933. She complained that about 3 weeks prior to her admission to the hospital she experienced the gradual onset of cramp-like lower abdominal pain associated with nausea and vomiting. Abdominal distention became noticeable. Vomiting, which at first was bile-stained, later became feculent. Constipation was noted although the patient had slight bowel movements with enemas. The past history was apparently negative except for an attack of pain in the left kidney region associated with dysuria and frequency, about 3 months previously. She was treated at that time in another hospital for pyelitis.

Fig. 13. Roentgenogram taken after a barium meal shows the terminal ileum narrow and irregular in outline, and bent in the form of a letter "U." There is a filling defect in the head of the cecum.

Fig. 14. In this roentgenogram taken after a barium meal, a constriction or a "napkinring" filling defect of the terminal ileum with dilatation of the ileum proximal to the defect is demonstrated.

Physical examination showed a well nourished, white woman who appeared acutely ill. The temperature was 99 degrees F.; pulse rate, 96; and respiratory rate, 20. Abdominal examination showed a moderate distention, particularly over the lower abdomen. There was visible peristalsis which was associated with an increase in the peristaltic sounds (borborygmi). There was diffuse tenderness over the lower abdomen, particularly on the left side. The general physical examination revealed nothing of apparent importance. The white blood count was 16,800. A diagnosis was made of subacute small intestinal obstruction.

The patient was operated upon October 18, 1933. An orange-sized mass was found in the lower abdomen. The mass consisted of loops of small bowel and omentum which were adherent by fibrin. Several loops of small bowel were dilated to about 5 centimeters in diameter, whereas, others were about 2 centimeters in diameter. The dilatation of the bowel appeared to stop about 2 meters from the ileocecal valve. The wall of the dilated bowel was edematous, thickened, and measured about 5 millimeters in thickness and appeared subacutely inflamed. Upon separating the loops of intestine and omentum that comprised the mass, an area of constriction was found about 1 centimeter long, which seemed practically completely to obstruct the lumen. There was fistulous communication between a loop of unobstructed small bowel and the dilated intestine just proximal to the site of obstruction. A V-type of resection of the obstructed area, including the fistulous opening was performed without cutting the mesentery. The bowel was reunited by an end-to-end anastomosis. After operation the patient was given a transfusion of 500 cubic centimeters of whole blood. Her subsequent course, except for a wound infection, was uneventful.

Histological examination of the excised pieces of bowel showed a marked thickening of the bowel with chronic inflammatory granulation tissue non-specific in nature.

SUMMARY

Eight cases of regional enteritis, one of the jejunum and 7 of the ileum are reported.

Four of the patients had acute regional enteritis. In 3 the process resolved spontaneously and in 1 it progressed to the chronic stenotic phase.

There were 4 cases with the chronic stenotic type of regional enteritis. Two had lesions of the terminal ileum. One patient who had a lesion of the terminal ileum complicated by a large abscess and developed following drainage of the abscess a persistent external intestinal fistula which required resection. The fourth case had a regional jejunitis.

The pathological anatomy is that of a non-specific inflammation. The acute regional enteritis consists of an infiltration of the bowel wall by an acute inflammatory granulation tissue with

extensive ulceration of the mucosa. This process may resolve spontaneously or progress to the chronic phase. The chronic forms of regional enteritis are usually associated with a hyperplasia of the intestinal wall by a non-specific inflammatory granulation tissue which contains granulomas, foreign body giant cells, and an excessive amount of connective tissue. Linear ulcers of the mucosa are present along the mesenteric border of the bowel. In the terminal ileum these ulcers penetrate through the bowel wall and form sinuses that lead into the mesentery which is frequently the site of an abscess. Internal and external intestinal fistulas may develop and lead from the involved intestine to an adherent loop of bowel or abdominal wall. The pathogenesis of this regional inflammation of the intestines is not known. Clinical and pathological studies have failed to demonstrate any evidence of tuberculosis, actinomycosis, syphilis, or Hodgkin's disease.

The symptomatology of regional enteritis varies with the different phases of the pathological process and with the location of the lesion. The symptoms in the acute types of regional enteritis, particularly of the ileum, usually simulate an acute appendicitis. The symptoms in the chronic forms mimic a low-grade intestinal obstruction or ulcerative colitis. Persistent external intestinal fistulas develop following drainage of an intra-abdominal abscess which is a sequel of the regional enteritis. The lesions higher in the intestinal tract tend to give symptoms of an intestinal obstruction more frequently and more rapidly than lesions in the ileum or colon. The diagnosis in the acute types of regional enteritis is usually made at operation undertaken for an acute appendicitis or an "acute surgical abdomen." In our series of cases the symptoms in the patients with an acute regional enteritis were those of an acute incomplete intestinal obstruction. The physical findings corresponded closely to those of an acute appendicitis. This association of symptoms and physical signs of acute intestinal obstruction and acute appendicitis may be an aid in establishing the diagnosis of an acute regional enteritis. The diagnosis of chronic types with stenosis of the bowel is usually made by roentgen examination which shows a filling defect in the involved intestine.

The treatment of regional enteritis varies with the phase of the pathological process. Acute regional enteritis limited to the bowel and not associated with thickening of the mesentery may resolve spontaneously. If, however, the mesentery is thickened and indurated, it is probable that ulceration of the mucosa has extended into the mesentery; spontaneous resolution then is less likely to occur, and a shortcircuiting operation or a resection is indicated. Chronic regional enteritis with stenosis is best treated by resection or a shortcircuiting operation. When complicated by an external intestinal fistula, resection of the involved bowel with the fistulous tract is necessary to close the fistula.

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THE TREATMENT OF ABORTION

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THE accidental or criminal termination of a pregnancy in its early months results in a condition which frequently offers a serious problem in treatment. Nor is it uncommon for an ethical physician to be called upon to administer to a patient upon whom a criminal abortion has been attempted or partially completed. When such a situation arises, it becomes his duty to treat such a patient and do whatever may be possible to spare her. If the abortion should be accidental, he must likewise be prepared to handle the case in the most rational manner. Many factors may arise in the individual case which make it necessary to exercise extreme judgment in its management. It would seem that the importance of selecting the proper procedure in these cases has been emphasized too little. Obviously no definite steps may be set forth which can be applied to all cases; but certain definite principles have been accepted, more or less, which may be applied to the advantage of the patient. It seems appropriate, therefore, to present a study of the various types of abortion which have been observed at Cleveland City Hospital, the method of management, and the results obtained by such treatment.

This study represents a total of 445 cases which were observed at Cleveland City Hospital during the 2½ years from July 1, 1932, to January 1, 1935. A more or less uniform practice in the treatment of the fairly large series of cases, which were seen during this interval, affords an excellent opportunity for appraisal of results. No therapeutic abortions or threatened abortions are included. In a number of instances, the differential diagnosis presented some difficulty; but no cases are included in which the diagnosis of abortion was not proved by definite clinical evidence or positive pathological findings. In several cases a definite diagnosis was not established before postmortem examination. It is reasonable to suppose that many of the abortions were accidental or spontaneous, but it probably would be conservative to estimate that 70 per cent or more were induced by some sort of intrauterine manipulation. Because of the unreliability of histories obtained, no exact figures concerning this are presented. That there should be great variation among the individual cases of such a series is obvious. In fact, when viewed from a distance, the whole series represents a rather bizarre aggregate from which to draw any convincing conclusions, but certain constituents appear in the study which are worth noting.

CLASSIFICATION OF CASES

Any termination of pregnancy before the end of the twenty-eighth week of gestation is classified as an abortion and is included in this series. If the abortion took place the first 16 weeks of the pregnancy, it is spoken of as an *early abortion;* if it occurred between the sixteenth and twenty-ninth weeks, it is termed *late abortion.*

Incomplete abortions. Any case in which reasonable evidence could be obtained to show that part of the products of conception had been expelled before admission, fits into this group. These constitute by far the largest group in the series with a total of 325 cases, 275 of which were early and 50 late.

Complete abortions. This group is represented by those cases in which the contents of the uterus have been completely expelled before admission, as proved by exploration of the uterus or substantial clinical evidence. Occasionally these patients are grossly infected, but most in this series provided no serious problem of treatment. There were a total of 50 cases, of which 40 were early and 10 late.

Inevitable abortion. An abortion is classified as *inevitable* when none of the products of the pregnancy have been expelled before admission, but in which instance the pregnancy is terminated during the hospital stay. Here, there arises the added responsibility of preserving the pregnancy if such is possible without endangering the health of the mother too greatly. In all, 70 such cases were observed. Of these, 41 were early and 29 late. Spontaneous completion took place in 20 of the early cases and 18 of the late cases, while in 21 of the early cases and in 11 of the late cases operative completion was required.

TREATMENT

Needless to say, much controversy exists regarding the treatment of the patient who presents herself with evidence to indicate that an abortion is pending or in progress. Many factors are to be considered, but the outstanding point of discussion is whether or not the uterus should

be invaded and the abortion completed when evidences of uterine infection are present. Much has been said against any such operative intervention when active infection is present. There are those who maintain that in the presence of fever and/or malodorous discharge, conservative measures of a supportive and palliative nature should be followed strictly. However, when the various types of cases are considered, it will be seen that to empty the uterus without too much delay will possibly be of great benefit in certain cases. Foremost of these are those instances in which hemorrhage may be so profuse as to be an immediate danger to the life of the patient. This usually occurs when the products of conception are separated from the wall of the uterus but not expelled from its cavity. To remove this material allows the uterus to contract and the bleeding ceases. It is notable, also, that many patients entirely fail to respond to palliative measures. In these, it becomes obvious that the presence of the necrotic infected material in the uterus, from which absorption is continually taking place, is working to the detriment of the patient. Often removal of this necrotic tissue results in a spectacular crisis and a rapid return to normal. From an economical standpoint, to empty the uterus at the earliest time when it may be considered safe, considerably shortens the patient's hospital stay.

Although it may be desirable to complete an inevitable or incomplete abortion as soon as possible, it must be kept in mind that to invade the uterus in the face of active infection is not without certain danger to the patient, as will be shown later. It is probable that in certain situations, this added risk is justifiable. Also, it will be pointed out that there is most likely an optimal time to complete the abortion even after the infection has subsided. It is rightly emphasized that when an infected uterus is subjected to the trauma of operative procedure, the so called "leucocytic barrier" is broken down and a spread of the infection made probable. Likely, the danger of such is greater when the invading organism is the hemolytic streptococcus.

General procedure. At Cleveland City Hospital, during the interval covered by this study, the general treatment of these cases has been fairly uniform. Often the patients admitted are in serious condition, many being severely exsanguinated, extremely toxic, or even moribund. First attention is always directed to supporting the patient generally. Fluids are given in whatever way may be possible. If anemia is marked, preparations are made for transfusion. Usually, unless it is thought that the abortion is only threatening, oxytocics are administered at once. These tend to check bleeding and probably lessen "toxic" absorption. As a rule the patient is given every opportunity to complete the abortion spontaneously. When the uterus has contracted firmly, gentle but firm suprapubic pressure may serve to express the secundines completely. If this is unsuccessful, it is preferred to do no more to the patient for 24 to 48 hours.

TABLE I.—SUMMARY SHOWING MANAGEMENT OF 445 CASES

	Cases
Abortion at time of admission	50
Spontaneous or non-operative completion after admission	107
Operative completion	
Dilatation of cervix and curettement	93
Dilatation of cervix and removal of tissue, only	40
Curettement, without dilatation of cervix	54
Removal of tissue without dilatation or curettement	85
Died with abortion incomplete	16

Afebrile abortions. If not complicated by serious blood loss, these cases are easily managed. Often the abortion is spontaneously completed within 48 hours. If such is not the case, the uterus is emptied by the least traumatizing procedure. Usually this can be done without further dilating the cervix and without using the sharp curette. Our experience has shown that this can be done without being followed by serious morbidity.

Infected abortions. These may include any case, from that showing a slight elevation of temperature and few constitutional symptoms, to the acutely ill patient with chills and fever; or slight fever and an extreme degree of prostration. When first seen, it is usually impossible to predict the ultimate course of the process; but it is noteworthy that the patient who shows slight or no fever, low blood pressure which cannot be explained by blood loss, feeble pulse and extreme prostration, almost always responds poorly to all therapy. It can strongly be suspected that this patient harbors an infection of virulent streptococci, and all intra-uterine manipulation positively should be avoided. Less concern should be felt for the patient who shows high fever, chills, full bounding pulse, and who does not appear so ill. Here it probably may be considered that the uterus is invaded by the usual saprophytic organisms.

The infected case is generally treated "conservatively." If hemorrhage is not severe and the patient responds satisfactorily to palliative measures, time is allowed for the temperature to sub-

side. Frequent small transfusions of whole blood have proved excellent supportive treatment in patients with severe infection. When the fever has been lower than 100.4 degrees F. for 24 to 48 hours and it is felt that the uterus is not empty, operative completion is done.

TABLE II.—TIME OF SURGICAL INTERVENTION

Time of Intervention	Cases
Within 24 hours of admission	
Febrile	15
Afebrile	63
During febrile stage after 24 hours observation	47
Afebrile 24 hours	57
Afebrile 48 hours	38
Afebrile 72 hours or longer	49

Occasionally that case is seen in which it is felt advisable to empty the uterus in spite of an existing febrile state. Not infrequently the response is favorable, but it must be heeded that such a step definitely increases the patient's chance for morbidity, which may be serious. It must not be undertaken unless it is felt that the patient's general condition warrants such a risk. It will be seen in Table II that this was a not infrequent procedure in this series, but our morbidity rate in these cases is tending to result in fewer patients being handled in such a manner (Fig. 1).

Inevitable abortion. These cases are peculiar only in that an effort should be made to save the pregnancy, if possible. If active infection is present, treatment is as for other infected abortions, and oxytocics are given without regard for the pregnancy. If afebrile and the Friedman test indicates that the fetus is dead, the uterus is emptied without delay. Otherwise, the abortion is treated as *threatened*.

TREATMENT OF COMPLICATIONS

Treatment of the complications of abortion is necessarily highly individualized. However, some general observations as to the manner with which these are dealt, as they arise, would be in order.

Hemorrhage. Profuse bleeding, even to the point of exsanguination, is a common complication of abortion, and must at times be dealt with immediately. Temporary support of the circulation by means of intravenous infusions of normal saline solution, to which epinephrine may be added, is sometimes of great benefit. Solutions of isotonic glucose, or gum acacia, are administered in the more severe cases in order to support the patient while preparations are being made for blood transfusion. Blood transfusion was

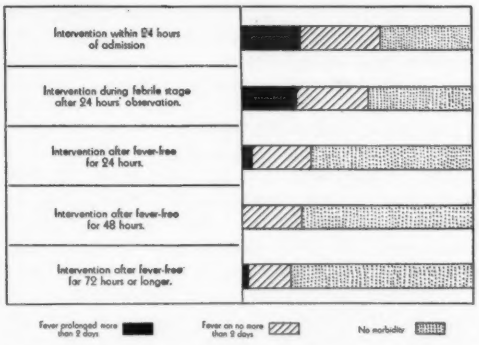
Intervention within 24 hours of admission
Intervention during febrile stage after 24 hours' observation.
Intervention after fever-free for 24 hours.
Intervention after fever-free for 48 hours.
Intervention after fever-free for 72 hours or longer.
Fever prolonged more than 2 days
Fever on no more than 2 days
No morbidity

Fig. 1. Illustrating the extent of the morbidity following operative treatment, with relation to the febrile state of the patient at the time at which the operation was done.

used freely in this series. As soon as a satisfactory donor can be secured and preparations completed, the patient is given 500 cubic centimeters of whole blood by the Vincent tube method. No serious reactions to transfusion were noted, and many patients were undoubtedly greatly improved by the procedure. Transfusion is usually considered indicated when the red blood cell count is below 3,000,000 per cubic millimeters, or when the patient shows signs of shock due to blood loss.

The hemorrhage occasionally necessitates early interference in these cases because of its severity. The usual methods to control hemorrhage are used, consisting of shock position, application of external heat to the extremities, ice bag to the fundus uteri, and the administration of ergot, pituitrin, and more recently pitocin. If bleeding continues in spite of these measures and the abortion does not complete itself within a few hours, the uterus is emptied, care being taken to cause as little trauma as possible. When done gently, this procedure should carry with it very little morbidity. Often it is not even necessary to administer a general anesthetic.

Sapremia. The less virulent infections, associated with abortion, have previously been considered to be "sapremic," and were thought to be brought about by putrefactive bacteria. A copious, malodorous discharge was thought to be characteristic of this condition which was formerly looked upon as an entity. Observations in this series would lead us to believe that the character of the discharge, *per se*, as well as the presence or absence of chills, does not differentiate between a relatively benign infection and one of more serious import. However, as pre-

viously stated, the patient with high fever, but not appearing very ill, has usually proved to have a mild type of infection. These patients are treated by bed rest in Fowler's position, application of heat to the lower abdomen, and the administration of oxytocics.

Septicemia. This unfortunate complication explained the death in a high percentage of the cases which terminated fatally. General supportive measures, fluids, and frequent small transfusions of whole blood, seem to be of the greatest benefit in such cases. Continuous intravenous drip has proved to be a valuable technique in the administration of saline and glucose solutions. In some instances "strepto-lysate" or "colo-lysate" were employed with some apparent benefit.

Endometritis. It is well known that there is considerable inflammation of the endometrium in all abortions whether they be criminal in origin or otherwise. Two very marked cases of endometritis were associated with placenta accreta. Endometritis is more commonly a preliminary infection, usually relatively mild, but occasionally is followed by other evidences of pelvic infection. It is very probable that all cases of "sapremia" are really examples of endometritis plus the presence of infected products of conception. The treatment is that recommended for sapremia.

Parametritis, pelvic cellulitis, and *pelvic peritonitis.* These are dealt with by giving the patient complete rest in bed, mild catharsis, abundant fluids, Fowler's position, and moist heat to the lower abdomen. The Elliott technique for administering pelvic heat is of outstanding benefit in these cases, frequently causing rapid resolution of the process, or aiding in the localization of an abscess.

Pelvic abscess. This was encountered occasionally in this series. Treatment is palliative until the abscess localizes and may be drained. Posterior colpotomy is the method of choice if the abscess is accessible by this route. Abscesses of the broad ligament are treated by Cullen's method of retroperitoneal drainage, unless pointing to the midline where they may be reached by pelvic puncture. In a few such cases dramatic results were obtained by posterior colpotomy when only a small abscess was evacuated.

Phlebitis. Elliott treatment and hot douches are found to be efficacious in cases of pelvic phlebitis. Phlebitis, or thrombophlebitis, of the femoral or saphenous veins is treated by elevation of the extremity under an electrically heated cradle. Prolonged bed rest is important in any case, together with support of the peripheral venous circulation by means of proper bandages or stockings when the patient is allowed out of bed. Hysterectomy is not done for pelvic phlebitis, and conservative measures are employed at all times. No instances of pulmonary embolus could be shown in the entire series.

TABLE III.—MORBIDITY OF OPERATIVE CASES

Reaction	Cases	Per cent
Febrile before completion; no morbidity after	106	39.0
Febrile before completion; morbidity after	51	18.8
Afebrile before completion; morbidity after	13	4.8
Afebrile; no morbidity	99	36.4
Died after operative completion	3	1.0
Total number operative cases	272	

MORBIDITY AND MORTALITY

A careful study of the morbidity and mortality in this group of cases furnishes the best denominator by which to evaluate the results of the method of treatment followed at Cleveland City Hospital. In order to measure such a variable as morbidity, certain arbitrary points must be accepted. Our term "morbidity" is taken as that suggested by Stander[1] to apply to the puerperium. A case is spoken of as having had "morbidity" when there has been a temperature rise of 100.4 degrees F., or more, on any two 24 hour periods following operation, excluding the first 24 postoperative hours; or when the temperature has remained elevated longer than 24 hours. The term "febrile" will be used to indicate the presence of a temperature of 100.4 degrees F. or more, but not in the same restricted sense as "morbidity."

Total morbidity. Of the 445 cases studied, 254 cases, or 57 per cent, were febrile at some time during observation. This does not include the small number of patients who showed a slight febrile reaction, after operation, but no morbidity. Among the 50 patients admitted as complete abortions 24, or 48 per cent, were febrile. Of those who completed spontaneously or merely with the aid of suprapubic pressure, 54, or 50.5 per cent, of the 107 cases were febrile. Table III shows the morbidity in the cases that were treated by some operative procedure. It will be seen that the morbidity and febrile reactions compare favorably with the group percentage.

Morbidity of operative cases. It is demonstrated in Table III that those patients who were afebrile before operation had very slight tem-

[1] Stander, H. J. Am. J. Obst. & Gynec., 1934, 28: 421.

perature reaction to the treatment. In a large number of patients who had fever before intervention there was no subsequent morbidity. Aside from 3 cases with fatal termination there was a total morbidity after operation of 23.6 per cent, which must be accepted as a relatively low figure. Obviously the morbidity and mortality were low in the operative cases because those patients who were in critical condition were rarely subjected to intra-uterine manipulation. However, it may further be pointed out that when done in properly selected cases, the danger from operative completion of abortion is relatively slight.

Morbidity and type of operative procedure. The morbidity following operative completion of an abortion appears to bear some direct relation to the manner in which the uterus was emptied.

Table IV illustrates the percentage of cases showing morbidity following various types of operative completion of abortion. It is noted that this is morbidity seen in patients who were afebrile for at least 24 hours before operation. It is outstanding that those cases in which the least was done showed the lowest morbidity in spite of the fact that these were most often the recently infected cases. When the uterus was emptied without dilating the cervix and without using a curette, the morbidity was only 3.5 per cent. Dilatation of the cervix and curettement of the uterine wall gave a morbidity of 7.7 per cent. A notable point in this study is that dilating the cervix carries with it a higher morbidity than gently curetting the uterus. It is not difficult to conceive the greater trauma associated with any method of forcible dilatation of the cervix. In spite of the small number of cases presented, it must be concluded that all unnecessary trauma and manipulation should be carefully avoided when invading the infected or potentially infected uterus. Even vigorous bimanual examination under anesthesia must be looked upon as capable of causing dangerous dissemination of the disease process.

Relation of morbidity to the time of surgical intervention. From our study, it would appear that the time at which an operative completion is done bears no little importance to the morbidity rate. Figure I shows the time, with relation to the febrile state of the patient, at which the completion was done and the resulting reaction. These cases were grouped according to those which showed no more than a temperature rise of 100.4 degrees F. or above on 2 postoperative days, excluding the first 24 postoperative hours; those which showed a temperature reaction more

TABLE IV.—MORBIDITY AND TYPE OF SURGICAL COMPLETION

Procedure	No.	Morbid	Per cent Morbidity[1]
Dilatation of cervix and curettement	91	7	7.7
Dilatation of cervix and removal of tissue, only	40	4	10
Curettement, without dilatation of cervix	54	3	5.5
Removal of tissue, without dilatation or curettement	84	3	3.5

[1] Patients were afebrile for at least 24 hours before operation.

extended than this; and those which showed less than the minimal reaction. The latter group were conceded to be without morbidity. It will be seen that the temperature reaction was greater and more often prolonged when operation was done while the patient was febrile. The high morbidity among those patients who had surgical intervention within 24 hours of admission may be explained by the fact that they had been observed too short a time to determine the presence of active infection. Consequently, a number of patients were operated upon who would not have been included had they been observed a longer time. Also, many of these abortions were completed because profuse bleeding made it imperative. The results of this study confirm our opinion that the optimal time to complete an abortion, if at all, is when the patient has been afebrile for 48 to 72 hours. Nothing is to be gained, usually, by delaying longer, and to invade the uterus earlier carries a greater risk for the patient.

Accidents of treatment. Perforation of the uterus occurred in only 1 case of those 272 which received surgical completion. In this case the posterior wall of the uterus was perforated with the Hegar dilator and omentum was delivered through the opening. The abdomen was not explored and recovery was uneventful. Patient was discharged after 14 hospital days.

Mortality. In this series there were 21 deaths, or a gross mortality of 4.72 per cent. This mortality is really low, when the type of case handled at City Hospital is considered. It is notable that many of these patients were moribund at the time of admission and that 7, or one-third, of the deaths occurred within 24 hours of the time the patient was admitted. The average number of hospital days for the fatal cases was 7.9, although 1 case was in the hospital 44 days. It is interesting to observe that in 12 of these patients, there was an admitted history of criminal attempt to induce the abortion, and in 1 other case there was postmortem evidence to

indicate that the uterus had been perforated before admission to the hospital. Only 3 deaths occurred following operative treatment in City Hospital. These are worthy of individual mention. In 1 there was a history of criminal abortion by means of packing the cervix with cotton on two occasions. On admission the patient was bleeding profusely, had high fever and chills, and appeared quite ill. A transfusion and dilatation and curettement were done immediately. Following operation the patient continued to become worse, developed a cellulitis of the buttocks, and died after 21 hospital days. There was no postmortem examination. In a second case, death occurred on the operating table after 7 minutes of nitrous oxide gas anesthesia. No postmortem examination was permitted. The third death resulted from profuse uterine hemorrhage some hours after the patient had been transfused and the uterus apparently emptied. Hemorrhage was profuse and sudden, and there was no time to complete a second transfusion.

SUMMARY AND CONCLUSIONS

1. A study of 445 cases of abortion observed at Cleveland City Hospital during a period of 2½ years is presented. Over this interval the method of treatment was fairly uniform and affords suitable opportunity for appraisal of results.

2. The general tendency in treatment is toward a policy of non-intervention. It is recognized that invasion of the uterus, especially in the face of active or potential infection, may be exceedingly hazardous. However, it is believed that circumstances justify this risk in some instances.

3. The importance of blood transfusion as a life-saving measure in extreme exsanguination and as a therapeutic procedure in the presence of infection is properly stressed.

4. Intra-uterine manipulation is avoided in all cases if practical. Opportunity is allowed for spontaneous completion unless hemorrhage is severe or other conditions warrant immediate intervention. However, if the abortion is still incomplete after the patient has been afebrile for 48 hours, it is thought that there is no advantage in delaying completion for a longer time.

5. Of the 445 cases observed, 272 were treated by some type of operative evacuation of the uterus. It is shown that the optimal time to empty the uterus, when infection has been present, is after the temperature has been below 100.4 degrees F. for 48 hours. It is important to carry out this procedure with a minimum of trauma, avoiding dilatation of the cervix and curettement if possible. When the uterus is emptied at the proper time in properly selected cases and with minimal trauma, the morbidity following operative procedures is not excessive and is of a benign nature.

6. This series presents a total of 21 deaths—a gross mortality of 4.72 per cent. One-third of these deaths occurred within 24 hours of the patients' admission to the hospital. Only 3 followed operative treatment at City Hospital.

7. It would appear from this study that the mortality and morbidity in accidental or criminal abortion could be reduced materially by more intelligent management of each case from its onset. Such management would include the following of certain principles which experience has shown may not be violated without ill results.

HYPERTHYROIDISM ASSOCIATED WITH MALIGNANT TUMORS OF THE THYROID GLAND

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IN the 249 cases of malignant tumors of the thyroid gland which have been seen at the Cleveland Clinic, the first impression of the examiner in 4.1 per cent of the cases was that a mild or a questionable hyperthyroidism was present. A closer study, however, shows that in only 2 instances was there any indication of hyperthyroidism as based on such objective criteria as persistent tachycardia or elevation of the basal metabolic rate in the presence of a history and physical findings consistent with hyperthyroidism. It is not unlikely that the apparent hyperthyroidism in these 2 cases and in similar cases that have been reported by others was the result of one of two factors: (a) changes incident to an increase of the patient's vascular bed; or (b) simulation of hyperthyroidism by some systemic disturbance incident to the presence of a large malignant tumor or its metastases.

The first of these mechanisms, i.e., the simulation of hyperthyroidism by an increase of the vascular bed, is illustrated by the following case in which a malignant adenoma of the thyroid had resulted in a huge, pulsating metastasis to the ilium. Although a forceful tachycardia, an elevated basal metabolic rate, and a history consistent with that found in cases of hyperthyroidism were all present, in all probability the patient did not have hyperthyroidism, for the entire picture could be explained on the basis of increased circulation through the large vascular bed of the metastatic tumor.

CASE REPORT

The patient was a woman 65 years of age who came to the Clinic on November 6, 1934, because of a tumor of the left hip. Since childhood, a large goiter which involved the right side and isthmus of the thyroid gland had been present, but its size had not increased for many years. Two and a half years before this examination, the patient began to notice pain in the left hip. Six months later, a tumor of the hip was observed, and at about the same time, the patient noticed an enlargement of the left side of her neck.

Preceding this examination, palpitation and tachycardia had been noticed. The patient had been more nervous than usual, had lost strength, and, despite a good appetite, she had lost 10 pounds in weight. There had been moderate hyperhidrosis, but no tremor, dyspnea, dysphagia, cough, or hoarseness. Recently, the tumor of the hip had given considerable pain, and it was for this reason that the patient sought aid.

Physical findings. Physical examination revealed a well developed and nourished woman (Fig. 1) whose appearance and behavior did not suggest the presence of hyperthyroidism. The pulse rate was 120, the blood pressure was 140 systolic and 75 diastolic, and the temperature was 99.4 degrees F. The skin was somewhat pale, the hands were warm and dry, and there was no digital tremor. No exophthalmos, lid lag, or widening of the palpebral fissures was present. Examination revealed a large, soft, colloid adenoma of the right lobe of the thyroid gland and a smaller equally soft adenoma of the isthmus. Involving the left lobe, there was an extremely hard, fixed, nontender mass 7 centimeters in diameter which presented the clinical features of a malignant tumor. The heart was slightly enlarged to percussion, and there was a forceful thrust at the apex. A blowing systolic murmur was audible over the entire precordium, but the heart sounds were regular and of good quality. The peripheral vessels were moderately thickened. The lungs were clear and resonant throughout. On the left hip, fixed to the ilium, there was a huge, expansibly pulsating, firm, non-tender mass the size of a football. A thrill and bruit were present over the entire mass; overlying veins were dilated. Pressure on mass did not slow the heart rate. Patient walked with a distinct limp. Further significant findings not revealed.

Laboratory findings. The red blood cells numbered 4,130,000; the hemoglobin was 78 per cent, and the white blood cells numbered 8,500 with 62 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 23 per cent lymphocytes, and 14 per cent monocytes.

Urinalysis showed no sugar or albumin to be present, and only an occasional white blood cell was found. The fasting blood sugar was 104 milligrams, blood urea, 48 milligrams, and the carbon dioxide content was 54.8 milligrams per 100 cubic centimeters. On two separate occasions, the blood cholesterol was 185 and 182 milligrams per 100 cubic centimeters, and the blood iodine was 6.16 and 7.46 micrograms per 100 cubic centimeters. The Wassermann and Kahn tests gave negative findings.

A roentgenogram of the chest revealed the heart to be enlarged. There were several small nodules in both lungs which were interpreted as metastatic tumors, probably of thyroid origin. A roentgenogram of the pelvis (Fig. 2) showed a large, soft tissue tumor mass rising from the ilium. Destruction of the bone was so extensive that only a strip 1½ inches wide remained adjacent to the sacro-iliac joint. There was also an area of destruction of the ascending ramus of the left tuber ischii.

An electrocardiogram showed sinus tachycardia with normal rhythm, an inverted T wave in lead III, and left axis deviation. No evidence of myocardial damage.

The basal metabolic rates on three different days were plus 56 per cent, plus 29 per cent, and plus 26 per cent.

At the time of admission to the hospital, the patient's pulse rate was 130, and during the 7 days of observation, although the temperature was never above 99.5 degrees F., the pulse rate ranged from 100 to 110. The diagnosis at the time of discharge was malignant adenoma of the thyroid gland with metastases to the ilium, ischium, and lungs.

In this interesting case, many of the clinical features of hyperthyroidism were exhibited. The

persistent, forceful tachycardia, the palpitation, the increased pulse pressure, the loss of weight, the good appetite, the loss of strength, the nervousness, the basal metabolic rates of from plus 26 per cent to plus 56 per cent, and the recent enlargement of the pre-existing goiter all seemed to indicate that the neoplastic enlargement of the left lobe of the thyroid gland or its metastases were functioning as thyroid tissue and were inducing an active hyperthyroidism. The tachycardia could not be explained on the basis of respiratory obstruction, anemia, fever, or organic heart disease. Yet the blood iodine and the blood cholesterol on two separate occasions were well within the limits of normal—findings which must be interpreted as evidence against the presence of hyperthyroidism.

Since it could not be proved that the tachycardia and the increased basal metabolism in this case were secondary to hyperthyroidism, it is highly probable that they were the result of the increased action of the heart incident to the maintenance of the circulation of blood through the huge and excessively vascular, pulsating metastatic tumor of the ilium. It was assumed that the tremendous vascular bed of this tumor with its dilated vessels, pulsation, thrill and bruit had imposed so great a burden upon the heart that this organ was forced to increase its activity, thus resulting in a persistent tachycardia and in a mild cardiac hypertrophy. On this basis, the presence of the left axis deviation might also be interpreted as indicating that the left ventricle was doing an excessive amount of work. For the same reason, the total work of the heart was increased, and this increase resulted in increased oxygen consumption by the myocardium, and hence in an increase of the total oxygen consumption of the body and in a proportionate elevation of the basal metabolic rate. All clinical and laboratory findings in this case could thus be correlated on the basis of the increased work of the heart incident to the maintenance of circulation through so large a vascular bed.

Similar studies were made in the case of a woman 53 years of age who had a hypernephroma of the left kidney. The tumor was about 7 inches in diameter and presented an expansile pulsation as well as a palpable thrill and a loud bruit. There was a pulsating metastasis 2½ centimeters in diameter in the clavicle but X-ray pictures of the skull, chest, and spine revealed no further metastases. The pulse was consistently over 100 when the patient was at rest in bed, the blood pressure was 160 systolic, 70 diastolic, and duplicate basal metabolic rate determinations averaged plus 28 per cent. The blood iodine and cholesterol were within normal limits, and the appearance of the patient did not suggest the presence of hyperthyroidism. Since there was no fever and no abnormality of the blood, heart, or lungs to account for the persistent tachycardia, the increase of pulse pressure and the elevation of the basal metabolic rate, it was concluded that here again the increase of the vascular bed caused elevation of the basal metabolic rate.

In order to test this hypothesis, studies were made of a man 26 years of age who, for the past 10 years, had had a gradually enlarging arteriovenous aneurism of the carotid artery. The lesion was of traumatic origin and there was no associated disease or complication. This patient had a forceful tachycardia similar to that seen in the case just mentioned; the pulse rate ran as high as 120 and stayed consistently above 100 when he was at rest in bed. The blood pressure was 120 systolic and 65 diastolic. The basal metabolic rate on two occasions was plus 20 per cent, but the blood iodine was within normal limits (9.5 micrograms per 100 cubic centimeters) and there was no clinical evidence of hyperthyroidism. It is apparent that here the excessive work imposed upon the heart by an arteriovenous fistula, just as in the first case the excessive work incident to supplying a large dilated vascular bed, had resulted in a persistent tachycardia and in an elevation of the basal metabolic rate.

REVIEW OF LITERATURE

There is no agreement in the literature regarding the incidence of the association of hyperthyroidism with malignant tumors of the thyroid gland. Bérard and Dunet state that all the classical symptoms of hyperthyroidism are almost never seen in association with cancer of the thyroid gland, but they add that tachycardia alone is not infrequently observed and that tremor sometimes occurs. These authors state that exophthalmos associated with a malignant thyroid tumor has only very rarely been reported, and that they have not seen a single instance of such a case. In the American literature, a higher incidence of the association of hyperthyroidism with malignant tumors of the thyroid gland is reported. Simpson states that one-half his cases of malignancy of the thyroid gland have been associated with hyperthyroidism, and that he has seen 5 cases in which exophthalmos was present. Simpson concludes that in his cases, the "symptoms of hyperthyroidism have been produced by the secretion from the actively proliferating thyroid carcinoma cells."

Fig. 1. Photograph of patient.

Coller states that the commonest complaints in his series of cases of malignancy of the thyroid gland were of those symptoms which usually are associated with hyperthyroidism, such as nervousness, loss of weight, tachycardia and palpitation—symptoms which were present in 47 per cent of the cases. In 44 per cent of the cases, the basal metabolic rates ranged from plus 16 per cent to plus 80 per cent. Coller concludes, "The fact that most of these patients had basal metabolic rates that were normal or above normal suggests that malignant thyroid tissue may retain some of its original function."

Boothby found definite evidence of hyperthyroidism by a study of the basal metabolic rates in 22 per cent of 45 known cases of malignancy of the thyroid gland seen at the Mayo Clinic. Herbst, however, from the same clinic, could find clinical evidence of hyperthyroidism in only 3 per cent of the cases, and he states that there was no case of carcinoma of the thyroid gland in 5,867 cases of exophthalmic goiter.

Eberts (4, 5) has reported 2 cases in which active hyperthyroidism was associated with a malignant tumor of the thyroid gland, but he admits that the histology of these tumors was not typical

Fig. 2. Roentgenogram of pelvis showing large tumor and destruction of ilium.

of thyroid malignancy and states that since both patients were alive and well, 3 and 4 years, respectively, after operation, even more doubt is thrown upon the true nature of the tumor.

Pemberton concludes that the basal metabolic rate is influenced more by benign than by malignant tumors of the thyroid gland. He explains the occasional association of hyperthyroidism and malignant tumors by the fact that 87 per cent of the malignant tumors of the thyroid gland arise in adenoma which may or may not be associated with hyperthyroidism. This idea is in harmony with the findings of Marine and Johnson and of Eisen, who showed that in a series of cases of malignant tumors of the thyroid gland, metastasizing tumors did not exhibit the normal thyroid function of taking up and storing iodine.

Graham, in discussing tumors of the thyroid gland, has stated "It is the transformation of adenoma to carcinoma that constitutes the entity. The innumerable morphological variations possible in a series of tumors or even in a single tumor are but circumstances in the process." This interpretation of thyroid neoplasms would explain the occasional association of hyperthyroidism with a malignant tumor of the thyroid gland as representing the development of the malignant tumor in a previously "toxic" adenoma. However, there still remains the problem of reconciling the diverse opinions regarding the incidence of hyperthyroidism in malignant tumors of

the thyroid gland. Some writers place this incidence as low as 3 per cent and others as high as 50 per cent. It is my belief that misinterpretation of symptoms suggestive of hyperthyroidism, or differences in the pathological interpretation of tissues removed at operation are responsible for this divergence of opinion. Since a study of the pathological changes of the thyroid gland does not fall within the scope of this paper, I shall merely point out some mechanisms by which a malignant tumor of the thyroid gland can produce a clinical picture which closely simulates that of hyperthyroidism.

DISCUSSION

The type of tumor which attains sufficient size and vascularity to be able to produce systemic effects by overtaxing the circulatory mechanism as in the cases reported here must be relatively rare. It is nevertheless quite probable that a number of patients, in whom large vascular, malignant thyroid tumors and a secondary tachycardia were present, have been thought to have been suffering from hyperthyroidism and have been reported in the literature as cases of hyperthyroidism associated with malignant thyroid tumors.

The other type of case in which the presence of a malignant tumor is apt to result in a clinical picture that can be confused with hyperthyroidism is seen when there are systemic manifestations of extensive malignant disease. Pertinent data can be found in examining case records of malignant tumors of organs other than the thyroid gland. The history of loss of weight, nervousness, tremor, fatigue, and palpitation is unusual in the presence of any advanced malignancy. Since the presence of an advanced malignant tumor of any organ can result in a syndrome which suggests the presence of hyperthyroidism, it is not surprising that when the tumor involves the thyroid gland, hyperthyroidism is even more strongly suggested and the clinical picture is interpreted as the expression of a mild hyperthyroidism.

As has been stated, there are only two instances in a series of 249 cases of malignant tumors of the thyroid gland in which examination of the records shows any objective evidence of an associated hyperthyroidism. In the first of these 2 cases, the tumor was a large, rapidly growing, degenerating carcinoma so undifferentiated that it was at first considered to be a sarcoma. In this case, there is almost no possibility that the undifferentiated tumor tissue could have been able to function. It is probable, therefore, that the symptoms represented the systemic effects of extensive malignant disease or were the result of a coincidental overactivity of the uninvolved portion of the thyroid gland. Since the symptoms were very mild, since in spite of a single basal metabolic rate of plus 25 per cent the classical features of hyperthyroidism were not present, and since the remaining portion of the thyroid gland was in a pure colloid phase, the probabilities are that the clinical findings in this case were secondary to absorption from the large degenerating tumor or its metastases.

The second case in which hyperthyroidism appeared to be associated with a malignant tumor of the thyroid is an example of a malignant tumor developing in an adenoma which for several years had shown questionable signs of mild activity. The patient was a man, 56 years of age, who first had noticed nervousness and irritability in 1925, 2½ years before our examination. Enlargement of the neck was not observed until 2 years after the onset of these symptoms. In the 6 weeks prior to entry, he had lost 30 pounds in weight, and tachycardia, dyspnea on exertion, and tremor had developed.

Physical examination revealed the presence of a hard, nodular goiter of moderate size, tachycardia, and a slight, fine, digital tremor. A diagnosis of nodular goiter with moderate hyperthyroidism was made and ligations of both superior thyroid arteries were performed.

The patient returned 3 months later symptomatically unimproved. Subtotal thyroidectomy was performed and the pathological diagnosis of the specimen removed was malignant adenoma of the thyroid. The tumor was well differentiated and in addition, it arose in an adenoma, certain areas of which were definitely hyperplastic.

Following thyroidectomy, the patient made striking improvement and gained 38 pounds. Three months after the operation, in spite of the fact that no mention of recurrence of the patient's hyperthyroidism was made, the pulse rate was still consistently above 100 when the patient was at rest in bed. Bone metastases were discovered 2 months later, and the patient died with bone and pulmonary metastases 2 years after the thyroidectomy had been performed.

The evidence on which we based the diagnosis of hyperthyroidism in this case is not strong; yet the case is included because it presents the most clear-cut picture of hyperthyroidism that is to be found in the records of the 249 malignant tumors of the thyroid gland in this series of cases. In this case, there is no record of the basal metabolic rate, of the blood cholesterol, or of a blood iodine determination. Tachycardia was nearly as pro-

nounced after the operation as before, and soon after thyroidectomy, evidences of generalized metastases were seen.

As we have pointed out, great care must be exercised in making a diagnosis of hyperthyroidism in the presence of generalized metastases. It is, therefore, not improbable that this patient's symptoms were largely the direct result of the malignant disease rather than of a true hyperthyroidism induced by functional activity of the thyroid tumor and its metastases.

The basal metabolic rates in a recent series of 33 cases of malignant adenomas and of papillary carcinomas of the thyroid gland averaged plus 0.3 per cent. These two types of neoplasm are the most highly differentiated forms of thyroid malignancy and hence probably represent the type of tumor most likely to show functional activity. Yet in only 3 cases was the basal metabolic rate above plus 16 per cent. One of these 3 patients had an elevation of temperature associated with extensive pulmonary metastases. The second patient suffered from dyspnea secondary to tracheal compression; the third was the case herein reported in which a large pulsating metastatic tumor was present in the ilium. In no case was there clinical evidence of hyperthyroidism. In 4 cases, the basal metabolic rate was below minus 16 per cent. It has been found, therefore, that in this series of malignant tumors of the thyroid gland, there was no consistent deviation from the normal basal metabolic rate.

In conclusion, it can be said that in 249 cases of malignant tumors of the thyroid gland, there was not a single instance of the indisputable coexistence of hyperthyroidism. The rareness of the association of these two conditions suggests that this association is largely coincidental, the two diseases probably bearing no etiological relationship to each other. It must follow, therefore, that the diagnosis of hyperthyroidism should be made with caution in the presence of a thyroid gland which has the characteristics of a malignant tumor, and that, conversely, the diagnosis of malignancy should be made with equal hesitancy in cases in which there is unequivocal evidence of active hyperthyroidism.

SUMMARY

1. There is a lack of agreement in the literature regarding the incidence of hyperthyroidism associated with malignant tumors of the thyroid gland.

2. This disagreement can probably be explained (1) by differences in opinion among pathologists as to the criteria of thyroid malignancy, (2) the tendency, in the presence of goiter, to attribute to hyperthyroidism the symptoms and signs which are in reality the result of extensive malignant disease.

3. The mechanism whereby a large vascular tumor can produce a tachycardia, an increased basal metabolic rate, and a syndrome suggestive of hyperthyroidism is discussed, and a case is reported in which these findings were present.

4. There is no case in a series of 249 malignant tumors of the thyroid gland which shows a picture of unequivocal hyperthyroidism that cannot be explained as being the result of either (a) increased circulation through a large vascular tumor, or (b) systemic effects of extensive malignant disease.

5. The average basal metabolic rate of 33 patients with malignant tumors of the thyroid gland was plus 0.3 per cent.

6. The diagnosis of malignant tumor of the thyroid gland should be made with hesitancy in cases in which there is evidence of active hyperthyroidism.

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SKELETAL TRACTION AND COUNTERTRACTION METHODS

Used in Ordinary Extension Splints in Treatment of Fractures of the Long Bones[1]

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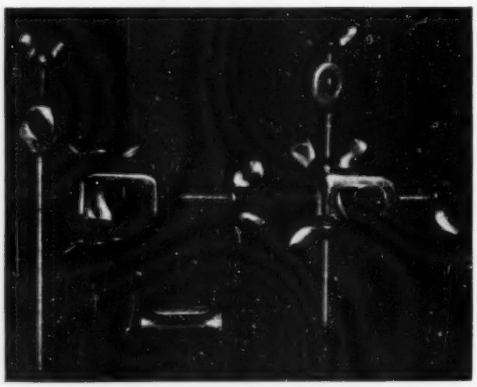
ALL of the present devices combining skeletal traction and countertraction are dependent upon a supporting frame, a part of the apparatus itself, to support the fractured extremity during the period of active traction and countertraction. Although these methods of treatment are excellent from a mechanical standpoint, there is one objectionable feature, the cost of the apparatus, which is due largely to the necessary supporting frame. The cost of the apparatus, therefore, is an obstacle to its general use by the average surgeon or hospital.

Because of the relatively high cost of the apparatus now in use, I have devised a more simple and economical means of applying skeletal traction combined with skeletal countertraction to ordinary extension splints. The simple and inexpensive device herein described makes this possible by utilizing only those extension splints commonly used in the average hospital. For this purpose one may use either a Thomas or Hodgen splint and the Bohler-Braun frame (2) for fractures of the tibia and fibula and for fractures of the femur, and the Clayton extension splint for fractures of the bones of the forearm.

My apparatus consists of two pairs of adjustable clamps, each clamp or unit being of similar pattern. Each pair of clamps serves to hold a transfixion pin or rigid wire in tautner to the supporting splint or frame. The pair of clamps holding the countertraction pin or wire in tautner are firmly secured to the rods of the splint or frame. The pair of clamps holding the distal or traction pin or wire in tautner are fixed to a sleeve placed over the side rods of the splint or frame. These sleeves to which the clamps are applied allow free play of the distal pin or wire in tautner while undergoing traction.

The apparatus is used with continuous traction by means of weight and pulley. It is the only device known to the writer to retain the principles of Buck's continuous extension with the exception of the "spring" traction in the apparatus of Hawley (4). This point is important because I am convinced that continuous traction by either weight and pulley or spring traction is superior to the so called intermittent or screw traction. This is particularly true of old fractures with shortening in which restoration of the length of the extremity can be obtained only by means of gradual and prolonged continuous traction.

The shifting proximally or distally of the clamps holding the countertraction pin or wire, together with the raising or lowering of opposite ends of



A B

Fig. 1. Photograph showing pin or tautner holding clamp with split sleeves; A, unassembled; and B, assembled.

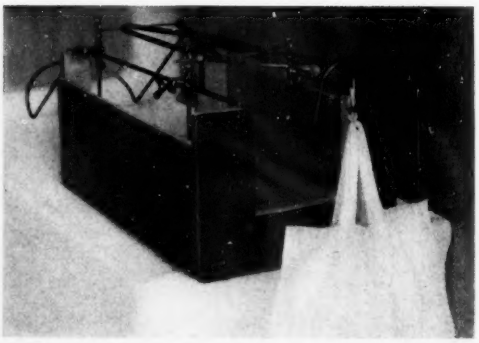


Fig. 2. Showing set-up with slightly modified Hodgen splint placed on an ordinary but cut out wooden box. This arrangement may be used instead of a suspended Thomas or Hodgen splint, a Bohler-Braun frame, or the new and more expensive apparatus used in combining skeletal traction and countertraction.

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Fig. 3. Case 1. Fracture of both bones of leg; treatment instituted about 24 hours after injury. Bohler pins inserted through upper end of tibia and the calcaneum and leg suspended in Thomas splint by means of the pin holding clamps. Continuous traction by means of weight and pulley. A non-padded plaster cast, incorporating transfixion pins applied 3 days later. See Figure 8 showing satisfactory reduction.

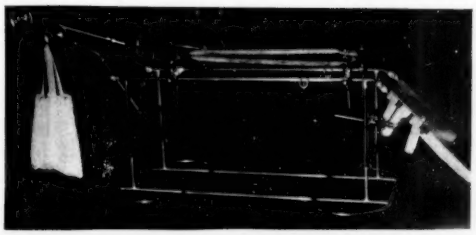


Fig. 5. Photograph showing Zimmer modification of Bohler-Braun frame to which have been attached pin or tautner holding clamps for skeletal traction and countertraction—continuous traction by means of weight and pulley.

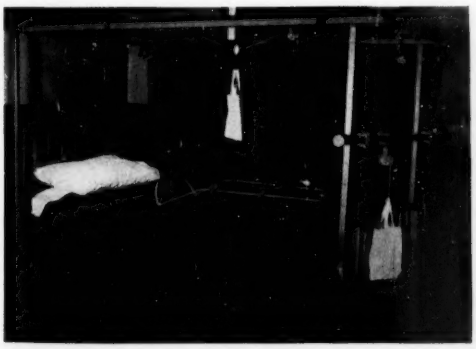


Fig. 6. Showing adjustable clamps attached to Hodgen splint suspended to overhead frame. This set-up is ideal for fractures of both bones of the leg as the splint provides for flexion of the knee.

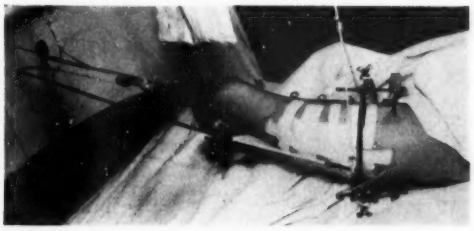


Fig. 4. Case 2. Fracture of femur followed by malunion (3½ inches' shortening and 40 degrees' angulation). Injury about 7 months before admission to hospital. Patient also had had an amputation below the knee on account of a compound fracture of both bones of the leg. The photograph shows the extremity suspended in a Thomas splint with an extra large ring piece and padding removed. The Bohler pins are seen inserted through the femur just below the trochanters and just above the epicondyles. Preliminary osteotomy separated the distal fragment from the third fragment firmly united to the upper fragment. Continuous skeletal traction of 30 pounds by weight and pulley with skeletal countertraction maintained for 12 days gradually restored full length to the femur (see Fig. 9, B). Then by open operation, interposing soft tissue was removed, reposition of the fragments was secured, and the third fragment, after osteotomy and only partial detachment from surrounding soft parts, was forced down alongside the ends of the major fragments with the idea of this third fragment serving as a bridge over the fracture site.

the traction and countertraction pins or wires greatly facilitates reposition and alinement of the fragments, an accomplishment similar to the Roger Anderson (1) and Griswold (3) splints. After satisfactory reduction of the fracture has been obtained, the clamps holding the distal or traction pin may be locked to the rods of the splint or frame, and the weights and pulleys

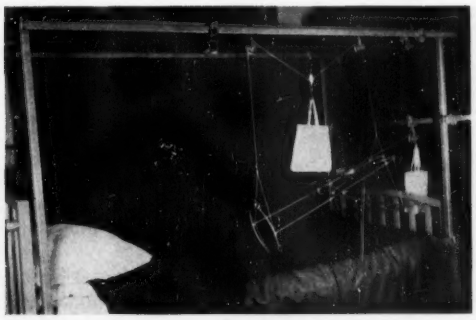


Fig. 7. Showing adjustable clamps attached to Thomas splint with an enlarged ring piece with padding removed and with Pearson leg attachment, suspended from overhead frame. This set-up is ideal for fractures of femur with marked shortening.

Fig. 8. Case 1. Roentgenogram of fracture of both bones of leg; before, left, and after treatment, right, with my device, showing perfect reposition of fragments.

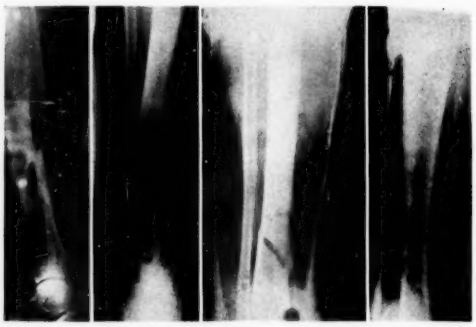
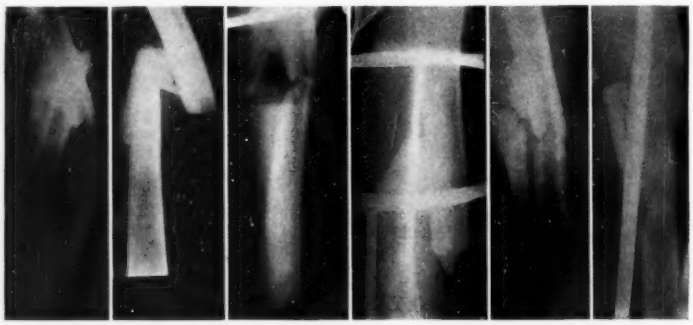


Fig. 10. Case 3. Roentgenogram of fracture of both bones of leg; before, left, and after treatment, right, with my device, showing perfect reposition of fragments. (Courtesy of San Francisco Hospital.)



A B C

Fig. 9. Case 2. Roentgenogram of fracture of femur followed by malunion; A, before preliminary osteotomy of distal fragment; B, 12 days later, restoration of full length by means of 30 pounds' continuous skeletal traction combined with skeletal countertraction; C, after open operation to remove interposing soft tissue and osteotomy of third fragment; continuous traction of 8 pounds by weight and pulley used to maintain the reposition and to immobilize the fragments.

removed. A non-padded plaster cast then may be applied to the extremity, incorporating the transfixion pins or wires. In compound fractures, the extremity may be left suspended for a longer period before encasement in plaster.

When my device is used with the Thomas extension splint, the skeletal countertraction eliminates the pressure of the ring piece against the ischial tuberosity, and also prevents an ill-fitting ring piece from pressing against the perineum. This greatly facilitates the use of the bed pan, simplifies the sanitary care, and adds greatly to the comfort of the patient.

The illustrations, Figures 1, 3, 4, 5, 6, and 7, showing the clamp unassembled and assembled, and as used with the Thomas and Hodgen splints and the Bohler-Braun frame, are self explanatory.

Roentgenograms with explanatory notes in three cases in which my device has been used are shown in Figures 8, 9, and 10.

SUMMARY

1. A description is given of a simplified and inexpensive apparatus to use with ordinary hospital extension splints for combining skeletal traction with skeletal countertraction for fractures of the long bones.

2. The apparatus is used with continuous traction by means of weight and pulley and is the only device known to the writer, to retain the princi-

ples of Buck's continuous extension with the exception of the "spring" traction in the apparatus of Hawley.

3. The apparatus is believed to furnish the best means of overcoming, after osteotomy, the shortening found in old malunited fractures of the long bones.

4. The apparatus, when used with the Thomas extension splint, eliminates the pressure of the ring piece against the ischial tuberosity, thereby simplifying the sanitary care and adding to the comfort of the patient.

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A METHOD FOR RE-EXPANSION OF THE COLLAPSED LUNG IN EARLY OR LATE EMPYEMA

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THE purpose of this report is to describe a simple, inexpensive method for passively re-expanding the collapsed lung in cases of early chronic empyema when no bronchial fistulas are present.

It is obvious, from a consideration of the physiology of respiration, that the degree of expansion of the lung is dependent on the balance of intrapulmonary and intrapleural pressures, mechanical factors such as elasticity of the lung tissues, pleural thickening and adhesions between the visceral and parietal pleura being considered as constant. This concept is utilized in the production of a partial or complete collapse of the lung in the induction of artificial pneumothorax in which instance the intrapleural pressure is increased. The reverse situation obtains in the respiratory exercises, such as forced expiration against pressure, used in the treatment of pleural empyema, in which case the intrapulmonary pressure is increased in an attempt to re-expand the collapsed lung. This, however, is an active procedure and has as the upper limit of a maintained increased intrapulmonary pressure the capacity of the respiratory muscles for work.

During normal inspiration the volume of the thoracic cage is increased so that the interpleural pressure becomes less than the intrapulmonic pressure and air rushes into the bronchi and expands the lungs. This process may be mechanically duplicated by the application of suction in the interpleural space so that the lung may be maintained in a state of continuous distention by the maintenance of a decreased interpleural pressure.

In cases of chronic empyema, the lung remains collapsed as a result of the presence of a complete pneumothorax (when the interpleural and intrapulmonic pressures are equal), and this collapsed state of the lung is also maintained by the presence of a thickened inelastic visceral pleura and possibly by changes in the elastic characteristics of the collapsed lung substance. If a pleural exudate is present, this will act further to compress the lung substance.

If, however, the interpleural pressure can be sufficiently reduced by continuous suction, the effect of the pneumothorax is overcome and the fibrous, thickened visceral pleura may be stretched so that the collapsed lung can be re-expanded.

METHOD

The source of suction is readily obtained by a modification of the Wangensteen suction apparatus (Fig. 3). A rubber suction cup attached as shown in the diagram is placed against the chest wall to cover completely the opening in the chest wall. The edges of the cup are ringed with petrolatum jelly. The clamps *A* and *B* are then opened, and the degree of suction applied is represented by the distance in centimeters of water between the water levels of the upper and lower bottles. The soft tissues of the chest wall are drawn outward into the cup, and the cup is maintained firmly in place by the difference between atmospheric pressure and the reduced interpleural pressure. After suction has established a constant level of interpleural pressure, clamps *A* and *B* may be closed and the suction cup may be separated from the suction apparatus

Fig. 1. Chest roentgenograms taken before and during the application of siphon suction at the left pleural space on May 17, 1935. The collapsed left lung and complete left sided pneumothorax with the drainage tube in place can be seen in the chest film before suction. After the application of siphon suction, shift of the left lung border outward and resultant decrease in size of left pleural empyema cavity, as well as shift of the trachea to left, can be seen.

Fig. 2. Chest film taken on July 12, 1935, showing complete re-expansion of the left lung and moderate thickening of the pleura.

at the rubber and glass tube junction. The decreased interpleural pressure may be maintained for several hours daily while the patient lies quietly in bed. If leakage of air should occur about the margin of the rubber suction cup, the subatmospheric interpleural pressure is increased to the atmospheric pressure level and the rubber cup falls off the chest wall.

The suction at first is started with the difference in water levels of the upper and lower bottles at 30 centimeters. With this degree of suction the patient may complain of a deep drawing sensation under the sternum which is very probably due to traction on the mediastinum causing displacement toward the side of suction. The lower bottle may gradually be lowered from day to day and the pressure in the interpleural space be made gradually more subatmospheric so that a difference in tension of 2 meters of water between interpleural and intrapulmonary pressures may readily be tolerated within 10 days to 2 weeks.

Between the periods of the application of suction to the interpleural space the lung partially collapses but the potential expansibility of the lung is gradually increased by stretching the thickened visceral pleura. The empyema cavity

becomes progressively smaller and is finally obliterated by the formation of adhesions between the thickened visceral and parietal pleura.

The contra-indications and possible dangers of the siphon suction treatment of early or late chronic empyema are:

1. The presence of a bronchial fistula, in which instance air rushes from the intrapulmonary to the intrapleural space, and suction cannot be maintained.

2. The possibility of hemorrhage resulting from sudden and excessive degrees of decreased interpleural pressure. To avoid any possibility of tearing small vessels or even the lung substance itself, the difference between interpleural and intrapulmonary pressures should be slight at first and gradually increased.

3. The possibility of a sudden marked mediastinal shift with torsion of the vessels at the base of the heart which may lead to circulatory disturbances. The mediastinum is, however, more rigid than normal in these cases and the possibility of a rapid shift is remote.

The method which has been described seemed worthy of trial since it had been determined on this service that the use of the suction side of the Drinker respiratory apparatus had been beneficial in re-expanding the collapsed or retracted lung. The method of continuous siphon suction for the treatment of chronic empyema has been used in a single case with results which appear worthy of a report.

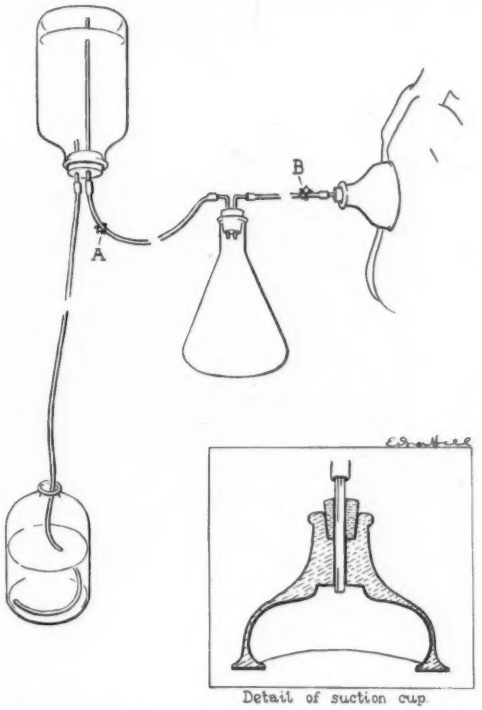

Fig. 3. Diagram of siphon suction apparatus and cross section of suction cup. The upper bottle is suspended from a stand and the lower bottle is placed on a table. The suction cup consists of a moderately firm rubber cup (sold in hardware stores to clean out clogged drain pipes) approximately 5 inches in diameter. A rubber cork is fitted into the cup and a hole is drilled through the cork and cup and a glass tube is introduced into the cup as shown in the cross section. This glass tube is connected by firm rubber tubing to the suction apparatus.

The patient, a white female 29 years old, viii-para in the third month of pregnancy, was admitted to the medical ward of the Hospital of the University of Pennsylvania, March 19, 1935. Two days before admission the patient had left pleural pain, dyspnea, and fever. Physical examination revealed signs typical of frank consolidation of the left lower lobe. Examination of the sputum revealed pneumococci subsequently identified as group IV. A diagnosis of left lower lobe pneumococcus pneumonia was made and confirmed by roentgen-ray examination. Artificial pneumothorax was induced and two refills were done within 36 hours with an initial drop in temperature and clinical evidence of improvement. The chest film after pneumothorax showed collapse of the left upper lobe and considerable mediastinal shift. Four days later there was a resumption of a febrile course and a chest film confirmed the clinical impression of the presence of a left pleural effusion. Repeated thoracentesis during the course of the next 2 weeks yielded purulent fluid which gradually increased in viscosity, and the patient was transferred to Surgical Service "E," April 6, 1935. Interrib drainage was instituted in the seventh interspace in the posterior axillary line on the left side and the Overholt modification of the Deryl-Hart apparatus was used for drainage. The purulent fluid became more viscid and on April 23, 1935, rib resection was performed and two drainage tubes were inserted. The empyema cavity was irrigated with Dakin's solution, and postural exercises and expiration against pressure by the use of blow-bottles were used in an attempt to re-expand the collapsed left lung. A chest film on April 30, 1935, revealed complete collapse of the left lung and some thickening of the pleura. In spite of the conventional exercises, there was little apparent change in the appearance of the chest on May 15, 1935, when continuous siphon suction was applied.

When suction was applied, the breath sounds were markedly increased in amplitude, and numerous râles were heard over the left lower lobe. These changes disappeared when suction was discontinued. The left lung was observed under the fluoroscope, and a definite degree of expansion occurred after the application of suction to the interpleural space. Chest films were taken before and during the application of suction (Fig. 1), and a definite shift of the left lung border outward away from the cardiac silhouette was observed. The superior mediastinum was shifted slightly to the left. With the continued intermittent application of siphon suction the left lung gradually re-expanded and almost completely filled the left thoracic cage at the time of discharge June 17, 1935. Three weeks

after siphon suction was started the wound was entirely closed and no drainage was present.

The patient was again examined on July 12, 1935, and roentgen-ray examination revealed complete obliteration of the left pleural space and moderate thickening of the pleura (Fig. 2). The site of the thoracotomy was completely healed and clinically the patient was well.

SUMMARY

1. A method for the application of siphon suction to the interpleural space to re-expand the collapsed lung in cases of early and late chronic empyema thoracis has been described.

2. The results of siphon suction therapy in a case of early chronic pleural empyema have been presented.

3. It is suggested that the method of siphon suction be used in cases of early or late empyema to re-expand the collapsed lung.

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AN ASEPTIC METHOD OF TEMPORARY VALVULAR ENTEROSTOMY[1]

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THE practice of performing valvular enterostomies has largely obviated the possibility of persistent fistulous formation. The desideratum, then, is a method whereby these intestinal stomas may be produced without exposing the peritoneum and abdominal wall to potential contamination by the intraluminary contents. This possibility, although rarely productive of lethal consequences, is nevertheless an ever present hazard and a decided factor in morbidity. Recent reports of the incidence and fatalities from gas bacillus infection complicating enterostomies are concrete illustrations (12).

Decompression of the intestine was deliberately done for relief of disease as early as the 16th century, when Ambroise Paré pricked the distended bowel with a needle for the purpose of assisting in the reduction of strangulated hernias (11). The success of this procedure, according to Saunders, probably suggested puncture of the intestine through the intact abdominal wall for relief of tympanites from any cause (11). This practice became widespread but seemed to find its greatest value as an euthanasic rather than a therapeutic measure, for Morgagni definitely pointed out in 1761 that should agglutination of the visceral and parietal peritoneal surfaces fail to occur, intestinal contents might escape into the abdomen and be the direct cause of a fatal result. In 1757, Lewis had recommended a more deliberate surgical procedure, but it was not until 30 years later that enterostomy, or enterotomy as it was formerly called, was first used by Renault, i.e., in 1787. The operation was revived by Nélaton in 1840, who devised a very ingenious method. The first loop of presenting distended intestine was sutured to the abdominal wound by two rows of interrupted sutures. It was opened immediately, or some hours later as the condition warranted. In this way, soiling of the peritoneal cavity was prevented. Thus it might be said that Nélaton established the technique of enterostomy.

However, it was the work of Fuhr and Wesener in 1886 of performing enterostomy for relief of ileus, with that of Schede in 1887 of sidetracking the fecal current during extensive operations on the intestine below (14), which marked the beginning of the era of temporary intentional fistulas. But closure of the stomas necessitated a secondary operation, either intraperitoneally or extraperitoneally for re-establishment of intestinal continuity.

Many surgeons have described numerous methods and established principles which have been utilized in circumventing this difficulty; among them being Moynihan, Lund, Lord, Lusk, Long, Horsley, and more recently Hendon. However, Eiselsberg, in 1895, was the first surgeon to apply the principles of the Witzel gastrostomy to enterostomy. But the procedure which seems to hold greatest favor and proves most uniformly successful is that described by C. H. Mayo in 1917. In this, the intestine is emptied of its gas and fluid content by compression with the hand, rubber covered clamps are applied to prevent gross spillage, and a rubber catheter is inserted and transfixed to the bowel wall. The tube is enfolded after the technique of Witzel, and a strip of omentum is interposed between the bowel and the anterior abdominal wall. Orr and others have

Read before the Indianapolis Medical Society, April 30, 1935.

supplemented this method by aspirating the contents of the distended loop by a fine needle. A solid tapered tip catheter has usually been preferred for enterostomy, instead of one with a hollow tip or plain rubber tubing, since insertion is facilitated and the wound in the intestine may be proportionately smaller; and the size originally advocated by Mayo was a No. 10 to 12 French. However, there is a constriction in the lumen of the standard commercial catheter which was found to retard the flow materially in a majority of a series examined. Therefore, the present tendency appears to be toward selection of larger sizes, namely Nos. 16, 18, or even No. 20, the advantage of the smaller tube being sacrificed in order to secure adequate drainage.

The method of temporary enterostomy now proposed requires the use of a length of No. 14 rubber catheter drainage tubing, to one end of which is attached a conical metal tip with multiple countersunk openings, and to the other a simple "slip-on" connector (Fig. 1). This size tubing was selected since a simple siphonage experiment demonstrated that drainage therefrom was as great as that from a No. 18 intact catheter and the addition of the metal tip did not materially decrease the flow. This rubber tube ensheaths a metal cannula, which in turn is occupied by a metal obturator with a trocar point (Fig. 2), the metal parts being of sufficient size to produce a "working fit" within the tube. The proximal end contains a simple coil spring and valve which render the instrument practically air-tight (Fig. 3).

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. Assembled instrument.

Fig. 2. Catheter with conical metal tip and metal connector, and metal cannula—disassembled.

Fig. 3. Longitudinal section of assembled instrument. *A*, Cone shaped valve. *B*, Simple coil spring, which when compressed causes the obturator to protrude through the metal tip, and upon being released causes retraction of the cutting point into the cannula.

An area of bowel wall approximately 1.5 centimeters in diameter is encircled by a pursestring suture, placed opposite the mesenteric border, attempting to catch a bit of the submucosa with each stitch. A second pursestring is applied in an opposite direction, immediately surrounding the first, the free ends of both being left long to serve as traction sutures. A single circular suture may be used; however, the two closely approximated concentric ones give greater security and ease of execution and do not utilize an undue amount of bowel. The tip of the instrument is placed in the center of the circumscribed area and held fairly firmly against the bowel at a 90 degree angle with the long axis of the intestine (Fig. 4). The elasticity of the wall permits burying of the conical portion of the tube as traction on the sutures is made. The first pursestring is drawn up and tied somewhat snugly around the base of the metal tip. The obturator is depressed, thereby puncturing the intestine, and then released, so that the bowel is protected from damage. The tube is guided with a rotary motion through the opening made by the trocar for a distance of 1 or 2 centimeters (Fig. 4, insert). The tautness of the bowel wall, and the right angle direction of the entering instrument will prevent any tendency toward separation of the muscular and submucosal layers of the intestine. The angle of the instrument is then changed to about 60 degrees from the norm in the cephalad direction, and it is again guided into the lumen of the bowel for another 1 or 2 centimeters, making a total of 3 or 4 centimeters (Fig. 5). The second pursestring is tied, and the ends of both cut short. The instrument is then depressed and made to parallel the long axis of the bowel, its rigid metal parts serving as a staff around which the bowel enfolds itself, thus facilitating the insertion of the continuous mattress suture. This suture should begin 0.5 centimeter distal to the point of exit of the tube, after the technique of Mayo-Witzel, and continue proximally for about 3 centimeters (Fig. 6). With this technique a decided inverted cone is produced, and the valve effect augmented with the tract lined by serosa to its termination (Fig. 6.

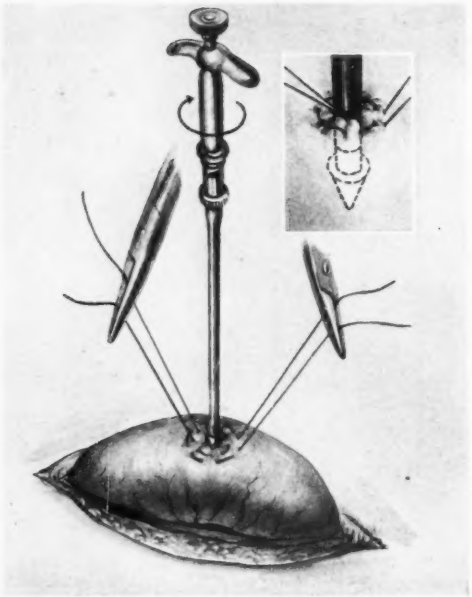

Fig. 4. Position of instrument and direction of traction on the sutures which facilitates invagination of the conical tip. Insert, Perforation of the intestine has been completed and the instrument guided into the opening.

insert). After the suture is secured, the needle arm is passed through a section of great omentum and parietal peritoneum near the wound edges and again tied, as described by Mayo. The

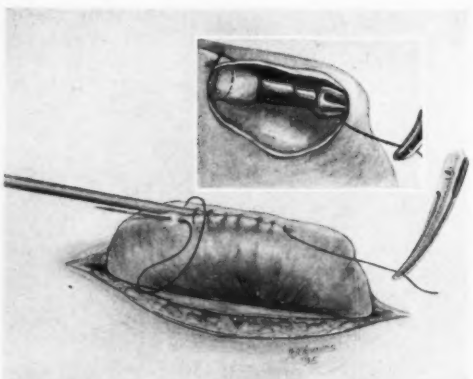

Fig. 6. Position of the rigid instrument which renders less difficult the application of the enfolding suture. Insert, Sectional view of the inverted cone.

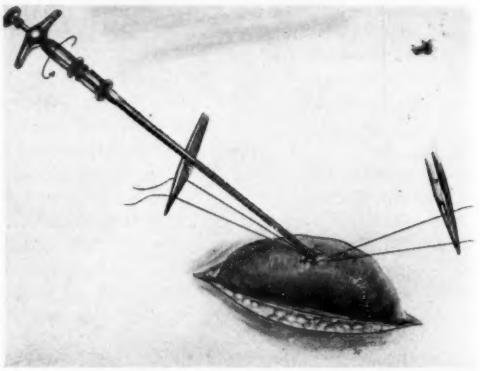

Fig. 5. The angle of the instrument changed to about 60 degrees from the norm, and it is being introduced somewhat farther into the lumen by a rotary motion.

wound is closed with interrupted sutures—the tube and instrument having been brought out through the dependent portion. A long strand of silkworm gut or silk is looped around the tubing at the point from which it emerges from the wound. It is tied with sufficient snugness to seat itself in the rubber, the ends being secured to the abdominal wall by adhesive plaster. This snubbing stitch may be passed through the skin; experience has shown, however, that it usually not only "cuts out" and delays convalescence, but produces an unsightly scar. The metal cannula

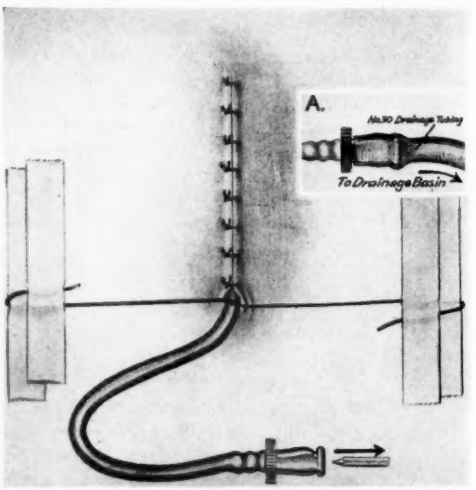

Fig. 7. Wound closed, the metal cannula removed from the tube; and the insert indicates the manner of connecting additional drainage tubing.

is then withdrawn from the tube and drainage established (Fig. 7).

It will be noted that in this technical procedure, rubber covered clamps, with the necessary "milking" of the intestine, are dispensed with. Sabin has shown that even in normal bowel there is mottling of the cytoplasm of smooth muscle fibers when clamps are applied, no matter how gently. This should stress the importance of minimizing traumatism at all times, but particularly whenever the bowel has become attenuated, poorly nourished and its permeability greatly increased from overdistension. For this reason, in those instances in which the intestine is so adherent as to preclude easy delivery of the segment from the peritoneal cavity, this method is particularly indicated. There is no necessity for anchoring the tube by transfixing it to the bowel, since the oblique position of the tube in relation to the long axis of the bowel is such as to overcome internal pressure, and the silkworm gut anchoring suture is protection against moderate external force. Further, by avoiding the transfixing suture, capillary drainage from a septic to a peritoneal surface does not occur, and the irregular opening produced by the "cutting out" of the suture with its accompanying delayed closure is prevented.

SUMMARY AND CONCLUSION

In conclusion, the advantages of this method are:

1. A comparatively small calibered tube is used, thus there is minimal encroachment upon the lumen of the bowel, yet adequate drainage is obtained because of the number of countersunk openings in the metal tip, and the uniform diameter of the lumen of the tube.

2. The instrument is simple in construction as it utilizes the old principle of trocar and cannula. The rubber sheath is standard size tubing and easily replaced.

3. Traumatism is reduced to a minimum by avoiding clamps, mobilization in adherent segments, and "milking" of the intestine.

4. Obviously, the serosal valve effect of the Witzel technique is assured, without nullifying any of the principles of modern intestinal surgery.

5. By avoiding aspiration of the distended bowel and the transfixing suture, and by completely isolating the proposed point of puncture by tying the pursestring suture around the tube while the intestine is still intact, the operation may be considered "closed" and thus aseptic.

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CLINICAL ASPECTS OF FIBROSARCOMA OF THE SOFT TISSUES OF THE EXTREMITIES[1]

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RECENTLY, a review was made of the histories and pathological specimens in all available cases of known primary malignancy in the soft tissues of the extremities, exclusive of lymphosarcoma, malignant myeloma, and epithelioma, in which the patients had been operated on at The Mayo Clinic during the 21 year period from January 1, 1910, to December 31, 1930. There were in all 232 cases in which pathological material was available for study. Of the pathological specimens, 152 (65.5 per cent) represent fibrosarcomas. Fortunately, as a result of an efficient follow up system, there are complete data in 138 (90.8 per cent) of these 152 cases.

It is the object of this paper to present the clinical aspects, briefly discuss the pathology, review the treatment, of fibrosarcoma, and to show the final results which have been obtained for a large group of patients observed over a period of 24 years.

INCIDENCE

In addition to these 232 cases there were 13 in which a diagnosis of sarcoma was made but in which no pathological specimen was available for study. Of these, 7 were originally called fibrosarcomas or spindle-cell sarcomas. In another case, probably of fibrosarcoma, exploration was performed, but no tissue was removed for diagnosis. Finally, it is estimated that about 24 probable fibrosarcomatous tumors, some of which had been proved by previous biopsy elsewhere, were seen but were not operated on. The total number of probable and proved fibrosarcomas of the soft tissues of the extremities, encountered during this period of observation amounts to 184, an incidence of 1 in 4000 patients.

ANATOMICAL DISTRIBUTION

The larger volume of the thigh and leg, as compared with the arm and forearm, is probably the chief etiological factor that determines the more frequent development of sarcomatous tumors in the lower extremity. In two-thirds of the cases the tumors occur in this region, and 43.4 per cent of the total number are situated near the thigh or knee.

The anterior parts are somewhat more prone to be involved than the posterior, and in the upper extremity the elbow region, especially the flexor surface, is the site of predilection. Particularly susceptible is the flexor surface of the thigh, for no less than a fifth of the total number of tumors are found in this situation.

In the 152 patients there were in all 160 primary sarcomatous tumors (Fig. 1). Fifty-six occurred in the upper extremity, 104 in the lower. There were 148 patients presenting solitary tumors; the upper extremity was involved in 51 cases, or 34.5 per cent, and the lower extremity in 97, or 65.5 per cent. In 4 cases, 2.6 per cent, true multiple sarcomas were present. In 3 (2.0 per cent), both the upper and lower extremities were involved; these, however, have been classified under the lower extremity, both as a matter of convenience and because this was the site of the tumor causing most concern.

GENERAL ETIOLOGICAL FACTORS

Sex. In fibrosarcoma, as in osteogenic sarcoma, males are much more frequently affected than females. Of the 152 patients, 102, or 67.1 per cent, were males and 50, or 32.9 per cent, females, a ratio of 2:1. In tumors of the upper extremity, approximately one in every four patients are women, while in tumors of the lower extremity, somewhat more than one in every three patients are women.

Age. Fibrosarcoma is a disease affecting chiefly those past middle life, 63 per cent of the patients with sarcoma being between the ages of 30 and 59 years. The average age incidence is 43.21 years, and the age of greatest frequency 45; 25 per cent of the patients falling in the age group between 40 and 49 years. Although no age is exempt, the least number of cases occur between the ages of

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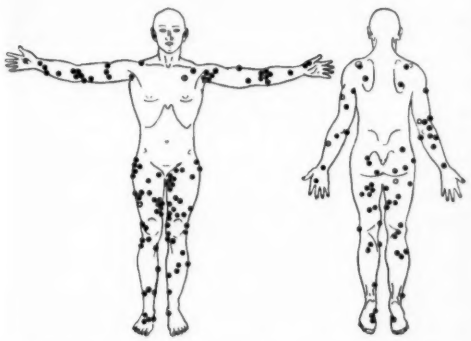

Fig. 1. Diagrammatic representation of anatomical situation of 160 primary fibrosarcomas of soft tissue, which affected 152 patients. The main sarcoma is represented by a solid black circle; the accessory primary sarcoma, by an outline circle.

10 and 15 years. The youngest patient in the series was a girl, 1 month old, who presented a congenital tumor of the foot; the oldest was a man 80 years of age. In 6, or 3.95 per cent of the cases, the fibrosarcoma occurred before the age of 10, whereas in 8, or 5.26 per cent, from the ages of 70 to 79 years.

The average age incidence for females is slightly greater than for males, and correspondingly, the age of maximal incidence is relatively increased. For males the incidence reaches its height between the ages of 40 and 45 years; for females, it closely approaches the fiftieth year.

Trauma. In the present series of 152 cases there were 102 in which no history of antecedent trauma was elicited. In the 50 remaining, or 32.9 per cent, some type of injury preceded the appearance of the tumor. In 31 of the cases there seemed to be little that would suggest more than an accidental association; however, the possibility must be borne in mind, even in these, that trauma may have been the exciting factor. Five of the 31 patients gave a history of sprain or strain immediately preceding the tumor. In these cases it is more likely that sarcoma was the cause, rather than the effect, of the "strain." Seventeen cases (11.2 per cent) are more convincing and are able to endure critical analysis. In all, the patients gave a definite history of trauma, followed within a reasonably short time by a sarcomatous tumor. These probably represent a true relationship between trauma and malignancies.

Heredity. Heredity seems to hold little if any position as a predisposing factor in the development of fibrosarcoma. In no case in the present series was a specific history of sarcoma elicited from any other member of the family. Of 135 patients whose family history was definitely recorded, 23, or 17 per cent, gave a familial history of cancer. This is considerably lower than the incidence given by Deelman in a study of the occurrence of cancer in the families of 250 noncancerous persons.

Fig. 2. Huge fibrocellular sarcoma of the thigh.

GROSS ANATOMY AND CHARACTERISTICS OF GROWTH

The subcutaneous and intermuscular tissues are the favorite sites for the development of fibrosarcomas (Fig. 2). Frequently these tumors are found densely adherent to tendinous aponeuroses and fascial envelopes, from which they manifestly spring. The cutis is a less frequent nidus, whereas occasionally an intramuscular source is clear. Rarely can a definite nerve origin be demonstrated, but not infrequently nerve trunks, as well as blood vessels and other structures, are completely surrounded by the growth.

These tumors are usually single, but occasionally arise primarily from multiple foci. They are rounded or lobulated, and are ordinarily sharply delimited from the surrounding tissues. The great majority grow expansively, the central portions increasing with the peripheral portions. This process may be modified by the appearance of a multicentric form of growth, probably determined by perivascular proliferation and giving rise to tumors not unlike large, multiple uterine fibromyomas. In extraordinary cases, an invasive character may be a prominent feature, the tumor

Fig. 3. Huge ulcerating, bleeding fibrosarcoma, grade 4, invading bone.

growing in the interstices and infiltrating the surrounding tissues.

The gross texture reflects the minute structure of the tumor. The highly cellular and vascular tumors are soft and present a homogeneous appearance on section. The fibrous growths are hard, non-vascular, and, when cut, reveal a fasciculated architecture produced by bundles of fibrous tissue traversing various planes. Edema, hemorrhage, mucoid degeneration, and cyst formation may be present, particularly in the softer, more cellular, tumors. In myxosarcoma, a soft, gelatinous, translucent structure recalls the nature of the growth.

Encapsulation is a characteristic feature of a large number of fibrosarcomas, 73 of the 132 tumors for which excision or amputation was performed being encapsulated. Small tumors generally have a delicate vascular investment of fibrous tissue adherent to their surfaces. With larger growths the enveloping tissue is often quite thick and firmly attached to the surrounding parts. Even though encapsulated, these tumors present a remarkable capacity for growing and molding themselves about structures; large arteries, veins, and nerves may be completely encased within a solid tumorous mass. These tumors may penetrate their capsule, absorb it, and invade surrounding tissues; however, a remarkable feature is the often present protective zone of fibrous tissue that is built up at the margin of the advancing tumor. This inherent protective mechanism is exemplified in many cases of secondary invasion of muscle in which, on microscopic study, a wall of connective tissue is seen to intervene between the healthy and involved portion of the muscle.

Bone (Fig. 3) may be thinned by pressure and, not infrequently, invaded and destroyed. In other instances, periosteal proliferation and cortical thickening, without actual involvement of the bone, may result from the irritation of the tumor. Muscle affords a favorite soil for secondary invasion, which is present in nearly all cases in which the tumors attain sufficient size. Destruction of skin, with ulceration, was a prominent feature in 23 cases. It may occur spontaneously or as the result of operative intervention, or it may occur from the application of cancer pastes.

Recurrent tumors are frequently single and, like the primary growths, are usually well circumscribed; frequently they are encapsulated. However, they may be multiple and be scattered throughout the tissues, and they may involve the parts some distance from the original growth although the usual site of recurrence is in the region of the previous operative incision.

MICROSCOPIC STRUCTURE AND GRADE OF MALIGNANCY

Fibrosarcoma presents a feature that constitutes a measurable indication of the normal functioning capacity of the cells, namely fibrogenesis. In other tumors of connective tissue type, osteogenic sarcomas and chondrosarcomas, the same power is manifest in the production of bone and cartilage, and the relative malignancy of these tumors is dependent on the amount of bone and cartilage they produce and the degree to which these products approach the adult type. In fibrosarcoma, however, there is no factor to indicate the relative adultness of the matrix, except in myxosarcoma, where the gelatinous groundwork recalls an embryonic structure.

However, the degree of malignancy of fibrosarcoma can be more accurately determined microscopically than for either osteogenic sarcoma or chondrosarcoma because the structure of fibrosarcoma is usually the same throughout the whole tumor, whereas the structure of the 2 other types not infrequently varies greatly in different parts of the same growth. Consequently,

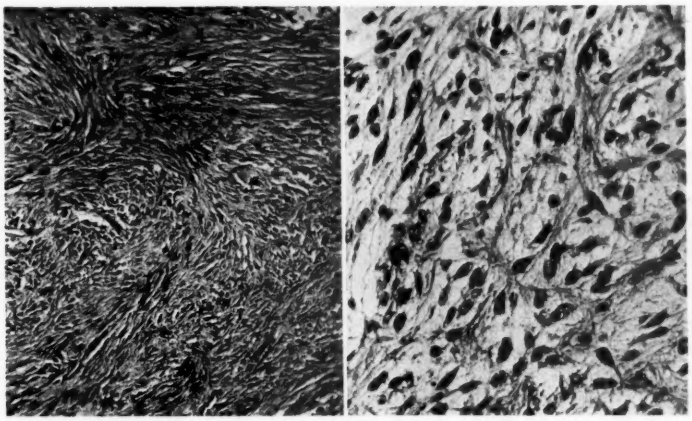

Fig. 4. a, left, Fibrosarcoma, grade 1, ×125; b, fibrocellular fibrosarcoma, grade 2, ×280.

considerable reliance can be placed on a given section of a fibrosarcoma, for it will usually reveal the nature of the bulk of the tumor.

The microscopic grade of a tumor is an index of the degree of malignancy. The customary plan of using four grades, according to the method devised by one of us (Broders), has been adopted, grade 1 indicating the lowest and grade 4 the highest degrees of malignancy. The amount of fibrogenesis, the relative proportion of fibers and cells, and the amount of differentiation of the cells, form the foundation for the grading of fibrosarcomas. Using these criteria, three types may be distinguished: fibrous, fibrocellular, and cellular (Fig. 4a).

The great majority of fibrous and fibrocellular tumors (Fig. 4b) are made up of large spindle cells which approach the fibroblast type; consequently, they are more or less differentiated. Their degree of malignancy is directly proportional to the number of mitotic figures and tumor giant cells which they exhibit. Fibromyxosarcomas, depending on the proportion of cells and fibers, may fall in either the fibrous or the fibrocellular group. The term fibrous fibrosarcoma of grade 1 means a slowly growing tumor, of a relatively low grade of malignancy, which is composed of cells closely approaching the fibroblast type and producing an abundance of collagen fibers. As the grade of malignancy increases, more and more tumors fall in the fibrocellular group. The term fibrocellular fibrosarcoma of grade 4 indicates a very highly malignant tumor, which exhibits numerous mitotic figures and a moderate number of collagen fibers.

The highly cellular sarcomas are all extremely malignant, which is exemplified by the undifferentiated nature of the cells, by hyperchromatism of the nuclei, and by scanty fibrogenic qualities. The relative number of mitotic figures is of little practical value in estimating the degree of malignancy of these tumors; furthermore, it is often misleading. There were only 4 cures (7 per cent) in 57 cases, and there was absolutely no relation between the number of mitotic figures present in the tumors and the final results obtained (Fig. 5).

Recurring tumors nearly always exhibit the same degree of malignancy as the previous growths, and in only a very few instances does a noticeable change take place. The dictum that with each recurrence the tumor frequently becomes more and more malignant is not substantiated by the present work.

For practical purposes, the fibrous and fibrocellular groups have been considered under one heading, for, as the index of malignancy increases, the fibrous group becomes replaced by the fibrocellular; thus, in grade 3, there were but 3 fibrous growths in a total of 23 tumors. It has been found, however, that the relative malignancy, determined by the number of mitotic figures, decreases slightly in inverse proportion to the number of fibers.

In 70, or 46 per cent, of the 152 cases the tumor was classified as grade 4, 65 of them falling in the cellular group. In the combined fibrous and fibrocellular group there were 87 tumors, 35 (40.2 per cent) of which were graded 2 and only 5 graded 4.

The age of greatest frequency is considerably lower among patients who are affected with cellular sarcomas than among those with fibrous and

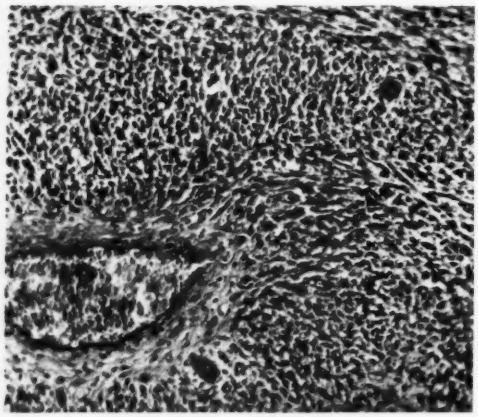

Fig. 5. Cellular fibrosarcoma.

fibrocellular tumors, the average age incidence being 36.5 and 48.2 years, respectively.

CLINICAL COURSE

The clinical course of fibrosarcoma is progressive, rapid, or slow, depending on the structure of the tumor. After local excision the disease usually recurs, and, with each recurrence, involves more and more of the surrounding tissues; eventually, it produces metastasis, or death from exhaustion, emaciation, or hemorrhage. Recurrences, as they progress in number, frequently come closer and closer together; occasionally, there is an increase in the rapidity of growth, although usually the same structure is exhibited.

In some cases, a small benign nodule of several years' duration may take on malignant change; in 9 cases small tumors had been present between 7½ and 35½ years before active growth began. Three of the tumors were of grade 1, 4 of grade 2, and 2, which were highly cellular, of grade 4.

Cellular sarcomas, although highly malignant, usually run a longer course than the less malignant fibrocellular tumors. Thus, of 104 patients who are known to have died as a result of the sarcoma, the average duration of life, from the onset of symptoms until death, for the cellular, and fibrous and fibrocellular types, was 82.9 and 67.7 months, respectively (Table I). Persistent recurrence after excision, and a tendency to metastasize to the lung is a characteristic feature of hyperchromatic spindle-cell tumors. Probably, in many of these cases the patients develop early pulmonary involvement, but, as a result of the slow progress of the disease, the pulmonary implants do not become prominent until late.

TABLE I.—DURATION OF LIFE OF 104 PATIENTS WHO ARE KNOWN TO HAVE DIED FROM THE SARCOMA

Type and grade of malignancy of tumor	Cases	Average duration of life, expressed in months from date of first operation at clinic until death	Average duration of life, expressed in months from onset of symptoms until death
Fibrous and fibrocellular			
Grade 1	12	37.25	110.16
Grade 2	19	17.52	70.31
Grade 3	15	22.06	43.2
Grade 4	5	13.5	29.3
	51	23.1	67.7
Cellular			
Grade 4	53	23.6	82.9

Pain, either local or radiating, was a prominent feature in 36 per cent of the cases. Referred pain, numbness, and partial or complete palsy indicate peripheral neuritis which is the result of pressure or actual invasion, and which may antedate the appearance of the tumor.

Fever, leucocytosis, and anemia are not characteristically associated with fibrosarcoma, and, when present, are usually the result of secondary infection, while loss of weight suggests long standing malignancy, or metastasis.

The demonstration of metastasis nearly always implies death within a few months; however, there was one remarkable case of a man, presenting a vascular, cellular tumor of the thigh, who survived 4 years and 7 months after the development of pulmonary involvement.

Intrathoracic pressure or pain, the onset of cough, and the expectoration of blood, even in the presence of a normal roentgenogram of the chest, nearly always indicate pulmonary involvement.

Invasion of regional or distant lymph nodes is an occasional feature of fibrosarcoma. Mediastinal, bronchial, and retroperitoneal lymph nodes are at times involved. Less frequent sites of metastasis are the skull, ribs, vertebræ, subcutaneous tissues, muscles, pharynx, and brain. Of the cases in this series, there were 5 instances of involvement of regional lymph nodes; 2 of these cases involved the axillary, and 3 the inguinal lymph nodes. Intra-abdominal metastasis, including involvement of the liver, was present in 15 cases, in 13 of which the disease was primary in the lower extremity.

Roentgenological examination of the parts (Fig. 6), if the tumor is large, usually reveals the

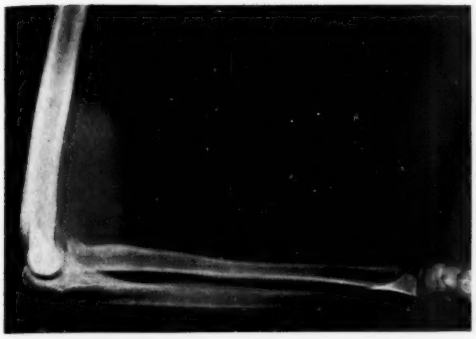

Fig. 6. Fibrocellular sarcoma of the arm. Metastatic growths were present in the lungs, ribs, nasopharynx, and subcutaneous tissues.

Fig. 7. Highly cellular fibrosarcoma which recurred, showing island of bone and bone marrow. Amputation was performed and 20 year cure resulted.

shadow of a soft tissue which occasionally reveals areas of calcification, which may lead to the erroneous diagnosis of angioma. Evidence of periosteal and cortical thickening, or actual invasion of bone is sometimes demonstrated, and was present in 28 of these cases.

A most important procedure is the routine roentgenographic examination of the chest, in every case of suspected malignancy, to determine the presence or absence of visible pulmonary metastasis.

TREATMENT

An estimation of the comparative value of the different methods of treatment of fibrosarcoma constitutes one of the greatest problems of surgery. Small primary tumors are properly treated by wide excision, which often effects a cure. In larger growths, the treatment of choice consists of excision or amputation, but the final result is dependent more upon the structure and inherent degree of malignancy of the tumor than upon any particular type of surgical procedure which aims to eradicate the disease.

If amputation were performed in every case a higher percentage of cures would be realized, but if this procedure were universally adopted, it is evident that many patients would sacrifice a limb unnecessarily; of the 28 cured patients in this series, only 6 had amputation performed. Amputation, on the other hand, occasionally effects a cure in cases in which excision is impossible or in which persistent recurrence demands its application. The results from amputation in these types of cases, however, are not good, and of 34 cases in which there were no demonstrable signs of metastasis, and in which amputation was performed at the clinic, there were but 5 cures (14.7 per cent). Furthermore, among 21 patients, who had had only 1 previous excision, there were but 3 cures (14.3 per cent). The grade of the tumor indicates the expected results, for in only 1 of the 5 cases, in which there was no demonstrable metastasis, and in which amputation resulted in a cure, was the tumor graded 4 (Fig. 7). In another case in which the tumor had been excised and graded 4, the patient had subsequent amputation performed and was cured.

In cases of involvement of muscle, wide excision through healthy muscular tissue, even to the performance of myectomy, depending upon the extent of the disease, should be performed. Even a group of muscles may be completely removed, and satisfactory functional results obtained. In cases in which secondary involvement of the nerves is present, it may be necessary to remove partially or completely a section of an important nerve.

The employment of mixed toxins of the Streptococcus erysipelatis and Bacillus prodigiosus appears to have a limited therapeutic value in the treatment of fibrosarcoma. Coley's toxin may produce some softening of the tumor and, at times, visible shrinkage; we use it, however, as an adjunct to surgical treatment. We have no evidence, in this study, of cure from the use of the toxin alone.

Radium and roentgenotherapy have been used with some success in certain sarcomas, chiefly the round cell, lymphocytic variety and in endothelioma. Fibrosarcoma, on the other hand, is a highly radioresistant tumor, though it occasionally responds somewhat favorably to radium or roentgenotherapy. The general treatment which has been adopted, in appropriate cases, is excision, followed by prolonged irradiation (Seyer-

TABLE II.—SARCOMA OF UPPER EXTREMITY; RESULTS IN 44 CASES ACCORDING TO TYPE, GRADE, AND SITUATION OF LESION

	Shoulder		Arm		Elbow region		Forearm		Hand		Total		Clinical cures, per cent
	D*	C†	D	C	D	C	D	C	D	C	D	C	
Fibrous and fibrocellular sarcoma													
Grade 1	0	0	0	1	0	0	2	1	0	1	2	3	60.0
Grade 2	0	0	3	2	2	1	3	1	0	1	8	5	38.5
Grade 3	0	1	1	0	2	0	0	0	0	0	3	1	25.0
Grade 4	1	0	0	0	1	0	0	0	0	0	2	0	00.0
	1	1	4	3	5	1	5	2	0	2	15	9	37.5
Per cent of clinical cures	50.0		42.9		16.7		28.6		100.00		37.5		
Cellular sarcoma													
Grade 4	2	0	7	0	4	0	5	1	1	0	19	1	5.0
Per cent of clinical cures	00.0		00.0		00.0		16.7		00.0		5.0		
	3	1	11	3	9	1	10	3	1	2	34	10	22.7
Per cent of clinical cures, total	25.0		21.4		10.0		23.1		66.7		22.7		

*D Died.
†C Clinically cured.

lein and Hoelzel, Wollner, Rostock, Hintze). In addition, Seitz and Wintz, and Quick and Cutler believe that pre-operative irradiation should also be employed. Regaud, Roux-Berger, and others concluded, from a study of nine fibrosarcomas, that roentgenotherapy is preferable to radium; none of their patients, however, was cured.

An intelligent evaluation of the therapeutic value of radium and roentgenotherapy in the treatment of fibrosarcoma is a very difficult problem. In the present series, the majority of patients who were subjected to excision of the tumor were given subsequent irradiation. This factor, together with the relatively small number of cured patients, makes the determination of beneficial results even more difficult.

An analysis of the results obtained by the different adjunctive methods of treatment, alone or in combination, is difficult to evaluate. An analysis of the case histories of the cured patients reveals little of note, except that there was a predominance of sarcomas of a low grade of malignancy. Of the 28 patients who were cured, 4 were treated by excision alone; 1 by excision and Coley's toxin; 17 by excision and radiotherapy alone, or in combination with Coley's toxin; and 6 by amputation.

There are no cases in which either roentgenotherapy or radium effected a cure of a definite recurrence. Irradiation does, however, occasionally produce a definite retardation of the growth of the tumor. Petersen's statement, that cures of sarcoma by roentgenotherapy are possible but extraordinarily rare, is borne out by the present work. Perhaps with earlier diagnosis, larger dosage, and improved technique, roentgenotherapy may, in the future, be of real benefit in the treatment of fibrosarcoma.

PROGNOSIS

The prognosis in a given case is dependent on the extent, situation, and duration of the disease; its rate of progress; the amount of invasion of surrounding tissues; the number of previous excisions; and, above all, on the cellular structure of the tumor. Situation, next to cellular structure, is the most important single consideration. Tumors of the lower extremity are more serious than those affecting the upper extremity (Tables II and III) and tumors of the buttock and thigh have an especially poor prognosis. Rapidity of growth usually implies a high degree of malignancy. Tumors which have been excised on several previous occasions usually have an unfavorable prognosis. Of the 28 patients who were cured, a conspicuous feature was the relatively high number of instances in which previous excision of sarcoma had not been employed (14 cases).

RESULTS

Of the 132 patients who either died as the result of sarcoma or were cured (Table IV) 28, or 21.2

TABLE III.—LOWER EXTREMITY; RESULTS IN 88 CASES ACCORDING TO TYPE, GRADE, AND SITUATION OF LESION

	Buttock		Thigh		Knee region and popliteal space		Leg		Foot		Total		Clinical cures, per cent
	D*	C†	D	C	D	C	D	C	D	C	D	C	
Fibrous and fibrocellular sarcoma													
Grade 1	1	0	5	6	2	1	2	0	0	0	10	7	41.2
Grade 2	1	0	9	2	0	1	1	2	0	1	11	6	35.3
Grade 3	1	0	4	0	3	0	3	2	1	0	12	2	14.3
Grade 4	1	0	1	0	0	0	1	0	0	0	3	0	00.0
	4	0	19	8	5	2	7	4	1	1	36	15	29.4
Per cent of clinical cures	00.0		29.6		28.6		36.4		50.0		29.4		
Cellular sarcoma													
Grade 4	2	0	17	0	5	2	4	1	6	0	34	3	8.1
Per cent of clinical cures	00.0		00.0		28.6		20.0		00.0		8.1		
	6	0	36	8	10	4	11	5	7	1	70	18	20.5
Per cent of clinical cures, total	00.0		18.2		28.6		31.3		12.5		20.5		

*D Died.
†C Clinically cured.

per cent, were free of disease for 3 years or more. Six other patients are living and either have the disease, or the period is too short to be of value in estimating the final results. The 14 additional patients, which bring the total number to 152, constitute a group in which it has been impossible to obtain reliable information concerning the final outcome; many of them have died; but the cause of death has been unascertainable. Of the 28 patients who were cured, 24 were free of disease for from 5 to 20 years; 18 from 5 to 10 years; and 6 from 10 to 20 years.

These cases, for the most part, represent a rather advanced stage of the disease. There was demonstrable metastasis in 9 cases at the time the patients registered at the clinic. In 20 other cases, the disease was far advanced, and biopsy alone was undertaken; the patients either refused amputation, or the situation of the tumor was such as to render its removal impossible. If these 29 cases are excluded as inoperable, the final number of cures, for operable cases, amounts to 27.1 per cent. This figure is extremely good, considering the length of time during which the patients were observed.

Pulmonary metastasis constitutes the chief cause of the fatal termination of fibrosarcoma, and, not infrequently, arises from tumors which have a relatively low grade of malignancy. Of 12 patients who had grade 1 fibrosarcoma, and who died as the result of the disease, no less than 5 are known to have developed pulmonary metastasis.

SUMMARY

A review of the primary malignant tumors of the soft tissues of the extremities, excluding lymphosarcoma, malignant myeloma, and epithelioma, which were treated operatively at the Mayo Clinic in 21 years permits the study of a relatively large number of cases, 152, and a follow up of 90.8 per cent, in which the diagnosis of fibrosarcoma was made. The history, the physical, laboratory, and surgical findings in these cases have been carefully studied and the pathological specimens have been examined again in order to reclassify and grade the degree of malignancy. Inasmuch as the patients in these cases have been seen over a period of 24 years, and because none of these have been observed for less than 3 years, the cases have been thought to be of sufficient value to permit certain conclusions.

The anatomical distribution revealed that in two-thirds of the cases, the growth occurred in the lower extremity, and that in about half of these cases, it was situated in the region of the knee.

The sex incidence disclosed that males were affected twice as often as were females and the average age in this group was slightly more than 43 years, but the range was from 1 to 80 years.

There was a history of trauma in 32.9 per cent of the cases; in 11 per cent of these cases, there appeared to be a true relationship between the injury and the formation of the tumor.

Heredity apparently had little bearing as an etiological factor; no patient gave a specific family history of sarcoma, although 17 per cent gave a history of carcinoma in the family.

Fibrosarcomas appeared encapsulated in 50 per cent of the cases and were usually single or lobulated and sharply defined in a layer of healthy connective tissue.

Bone was found to have been usually absorbed by pressure, but it may be invaded and destroyed.

Microscopically, fibrosarcomas are uniform in structure; therefore, sections removed at biopsy usually represent the true nature of the bulk of the tumor. The microscopic grade is an index to the degree of malignancy, grade 1 representing the lowest grade and grade 4 the highest grade of malignancy. The types of fibrosarcoma are fibrous, fibrocellular, and cellular; for practical purposes we combine the first two. The fibrous and fibrocellular types appear at a later age than does the cellular, and the latter type constitutes more than 90 per cent of growths in which the degree of malignancy was high, or grade 4.

The clinical course of the tumor, unless destroyed, may be rapid or slow and there may be recurrence after treatment. Recurrence eventually produces emaciation, exhaustion, metastasis, or hemorrhage and death. The roentgenogram reveals the first indication of pulmonary metastasis; in the extremity, the tumors cast a shadow which at times may be clearly outlined.

Treatment of the smaller tumors should consist of wide excision whenever possible. Surgical removal of large tumors may be impossible and amputation of the part may be necessary. Others are so situated as to make surgical treatment of little more than diagnostic value, and many tumors, which appear inoperable, have at biopsy proved to be of a low degree of malignancy and curable.

Irradiation alone has been resorted to in cases in which tumors could not be removed by excision or amputation, or in which the patient refused surgical treatment. Postoperative irradiation has, however, been used, and no doubt causes a delay in recurrence; it is difficult to evaluate the therapeutic benefits and, no doubt, with increased knowledge as to the dosage and improved technique, a more definite value as to the pre-operative and postoperative influence on the growth of fibrosarcomas will be arrived at. Our experience would indicate that these tumors are highly radioresistant and we are of the opinion that operation offers the more favorable result. The prognosis is chiefly dependent on the structure of the tumor and on the degree of malignancy. The more malignant the tumor, the more radical should be the treatment. Early amputation would result in more cures than are obtained otherwise, but the surgeon and the patient resort to it only after conservative measures fail. The proper co-operation of the surgeon, the pathologist, and the patient are essential for the best results.

TABLE IV.—RESULTS OF TREATMENT IN 132 CASES IN WHICH THE PATIENTS EITHER DIED AS THE RESULT OF SARCOMA OR WERE CURED[1]

Type and grade of malignancy of tumor	Cases	Clinically cured	Died	Cured clinically, per cent
Fibrous and fibrocellular				
Grade 1	22	10	12	45.4
Grade 2	30	11	19	36.6
Grade 3	18	3	15	16.6
Grade 4	5	0	5	00.0
	75	24	51	32.0
Cellular				
Grade 4	57	4	53	7.0
Total	132	28	104	21.2

[1]All of the 28 cures, with the exception of 4, have persisted more than 5 years. One patient has been free from symptoms for 3 years and 8 months; 1 patient for 4 years and 8 months; and 1 patient for 4 years and 11 months. In all probability all of these patients will pass the 5 year period. Another patient has been free of symptoms for 3 years.

We feel that microscopic examination of the tumor, in order to determine the type and degree of malignancy, is of great value in determining the type of surgical treatment advisable in each case. The surgeon, in determining the prognosis, must consider the site, size, duration, and rapidity of growth; the invasion of important structures, such as nerves and blood vessels; previous treatment, and pathological findings. Pulmonary metastasis is the most common cause of death and may occur in cases in which the grade of malignancy is relatively low. Nine patients revealed pulmonary metastasis at the time of their admission to the hospital. Twenty patients revealed evidence of advanced disease and biopsy alone was performed.

In our series of 132 patients, 28 (or more than 21 per cent) lived for 3 years following excision or amputation; 24 patients (17.5 per cent) survived 5 to 20 years; 18 patients (14.4 per cent) survived 5 to 10 years, and 6 patients (4.5 per cent) survived 10 to 20 years.

If we exclude the 29 cases in which the lesion was considered inoperable, or in which the patients refused operation, it is found that in 27.1 per cent of the cases, the patients survived for 3 or more years after the operation.

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EDITORIALS

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THE MECHANISM OF THE VERMIFORM APPENDIX—A POTENTIAL "CLOSED-LOOP"

THE alleged causes of appendicitis are multiple. Only two, however, have survived the crucial test of experimental inquiry, viz., infection and obstruction. Efforts directed at the establishment of the pathological picture of appendicitis in the cecal appendage of the dog have shown that these two factors must invariably be concurrently present in order to produce the disease.[1] High grade obstructions of the cecal appendage in the dog, when specific pyogenic organisms or feces are present in the lumen, are regularly attended by a process akin to that observed in appendicitis; when the lumen of the cecal appendage is washed, obstruction is not attended by significant consequence. The presence of pathological organisms without obstruction is equally well borne.

The investigations of Professor Aschoff[2] have lent the impression that appendicitis is essentially a specific bacterial disease after the manner of gonorrhea. He finds an enterococcus, more specifically a diplococcus type B, lurking normally in the distal one-third of the appendix, uncontaminated, in the main, by the more sociable organisms in the mixed flora of the proximal two-thirds. When acute suppuration supervenes, the diplococcus is found to be the predominant organism. The item of obstruction, he considers as being of no importance.

In 1846, in an admirable paper, too little known, Adolph Volz[3] relates the significance of appendiceal concretions for perforations of the appendix. When Fitz[4] in 1886 made the pronouncement that perityphilitic suppurations were caused by disease of the vermiform appendix, his words fell upon attentive ears. In a postmortem series of 152 instances of suppuration about the cecum, Fitz found an appendiceal concretion or foreign body present in 59 per cent of the cases. Van Zwalenburg[5] in 1904 and Wilkie[6] in 1914 reiterated faith in the belief that obstruction was a factor of major consequence for the occurrence of appendicitis. The force of the expressions

[1]Wangensteen, O. H., and Bowers, W. F. An experimental study of the significance of the obstructive factor in the genesis of acute appendicitis. Tr. Western Surg. Ass., 1935.

[2]Aschoff, L. Der appendisitische Anfall, seine Aetiologie und Pathogenese. Berlin and Vienna: Julius Springer, 1930.

[3]Volz, A. Die durch Kothsteine bedingte Durchbohrung des Wurmfortsatzes, die haeufig verkannte Ursache einer Gefaehrlichen Peritonitis, und deren Behandlung mit Opium. Carlsruhe: Chr. Fr. Mullers'schen Hofbuchhandlung, 1846.

[4]Fitz, R. H. Perforating inflammation of the vermiform appendix with especial reference to its early diagnosis and treatment. Am. J. M. Sc., 1886, 92: 321.

[5]Van Zwalenburg, C. F. Obstruction and consequent distension; the cause of appendicitis as proved by cases and by experimental appendicitis in dogs. J. Am. M. Ass., 1904, 42: 802.

[6]Wilkie, D. P. D. Acute appendicitis and acute appendicular obstruction. Brit. M. J., 1914, 2: 959.

of Professor Aschoff have, however, served to minimize the purport of obstruction and have lent increased credibility to the infection factor.

In describing perforation of the appendix in 1847, Gerlach[7] called attention to a mucosal fold which he described as a valve, interfering with emptying of the appendix. The existence of such a valve or of a sphincter has, however, been discredited by anatomists. That something of the nature of a sphincter-like mechanism uniformly exists at the base of the appendix, the writer has been able to demonstrate to his own satisfaction. In a series of many cases, in which the appendix was removed as an incident during another operation or in the interval when uninflamed, a needle attached to a column of water, was inserted into the lumen of the appendix at its distal tip. Resistance to the inflow of water into the cecum was consistently encountered—gravity pressures of 30 to 106 centimeters of water being withstood. In 17 instances, the mean pressure which was necessary to cause water to run into the lumen of the cecum was found to be 60 centimeters of water and the average was 56 centimeters. In instances in which appendectomy was done for acute suppurative appendicitis and a fecolith was found impacted in the lumen, attempts were made upon the excised appendix to dislodge the obstruction by the same means. Displacement of concretions by gravity pressure on the whole was found to be difficult. Rupture of the gangrenous wall by pressures in the range of the mean were not infrequent.

In two appendicostomies coincidentally done together with colostomy for cancer of the bowel, opportunity has been afforded during convalescence to measure the resistance to the inflow of water under the force of gravity. In both instances, the observed sustained pressure was found to be of the order of magnitude of the mean pressure noted in the acute determinations made during the course of appendectomy. Attempts at influencing with drugs the obstruction to the inflow of water through an appendicostomy have lent the impression that this resistance may be enhanced or diminished through such an agency. These observations made with the co-operation of my colleagues, Drs. W. P. Ritchie and R. Buirge, will be reported in detail elsewhere.

Those familiar with the potential hazards of experimentally closed intestinal loops will appreciate the latent danger inherent in this mechanism. In it one immediately sees an explanation for the stasis which gives rise to the formation of appendiceal concretions. These are laminated and usually free from bile pigments or biliary derivatives, though they have as a rule a small nucleus which comes from the intestinal canal. These concretions are found in most instances of perforative types of appendicitis. In the absence of an appendicolith, the mechanism which interferes with satisfactory evacuation may also initiate the changes which give rise to suppuration. Blood is pumped into the terminal arteries of the appendix under the motive force of systolic blood pressure; increase in intraluminal tension through the agency of physiological obstruction at the base of the appendix, precludes return of blood through the veins. Maintenance of this pressure-tension disturbance results in a struggle for hydraulic equilibrium. Rupture of venules occurs with resulting hemorrhage into the wall of the appendix. Oxygenation of the tissue suffers and the mucosa loses its miraculous ability to repel invasion of bacteria from the appendiceal lumen. Having been put in motion, this sequence of events can be arrested

[7]Gerlach, J. Beobachtung einer toedliche Peritonitis als Folge einer Perforation des Wurmfortsatzes. Ztschr. f. Rat. Med., 1847, 6: 12.

only by the obstruction giving way. The unusually generous distribution of lymphoid tissue beneath the mucosa and submucosa of the appendix is probably an important factor in determining the character of the inflammation which follows.

Man gives little promise of outgrowing this bad anatomical plan of the vermiform appendix. It appears most likely that the minute anatomy of the appendix is of more consequence than diet, latitude, longitude, or related factors in provoking the occurrence of appendicitis. If the obstructive mechanism at the base of the appendix, which makes of this narrow tubular viscus a potential "closed-loop", proves to be a sphincter, the significance of nervous influences becomes at once apparent. This little sword of Damocles always holds out a threat. Indications for its removal must not be too inflexible.

OWEN H. WANGENSTEEN.

THE GENTLE HANDLING OF CANCER

CELLS are carried from a cancer to distant parts of the body where they multiply and give rise to foci of new cancer growth. These cells are transported by the lymphatic current or the blood stream or by both in turn.

The lymph glands, interposed along the course of the lymph vessels, which drain the region of the primary focus of cancer, act as filters of the lymph stream flowing through them. Cells whisked off the primary growth lodge in the meshes of this lymph gland filter. When a number of cancer cells are suddenly carried into a gland by the lymph flow, some of them may escape and continue on with the lymph flow to be emptied into the subclavian vein.

Microscopic examination of the tumor is the only test we can use to learn whether the cancer in question belongs to the more malignant type or not.

The more the microscopic picture of a cancer resembles the normal gland in which it arises the more closely the cells cling to the framework structure of the tumor. Hence metastasis from this type of growth is delayed. On the other hand, if cancer cells are less differentiated into a structure resembling the normal gland and approach more the embryonic type of cells, then the more easily are they dislodged and carried off from the mother cancer.

Therefore, it behooves us in handling a tumor, e.g., of the breast, to be as gentle with our hands as possible lest we by roughness dislodge some cancer cells and hence be an accessory in causing distant metastasis.

If a microscopic examination of the tissue in question is necessary to establish the diagnosis, the method of obtaining this specimen must be carefully planned.

In a breast lesion it is better to excise the mass with a generous bit of the surrounding normal tissue or remove the whole breast if necessary, rather than cut into the tumor.

Trauma of the tumor itself by knife or needle is best avoided. Immediate cauterization of the biopsy wound in a tumor is merely locking the stable door after the horse is stolen. The location of the lesion, e.g., a prostatic or bronchial cancer, may necessitate a biopsy to establish a diagnosis. Biopsy handicaps the patient we hope to cure. One can readily see how tissue damage opens up both the lymphatic and blood vessels as well as dislodges cancer cells that may be carried elsewhere in the body.

In handling the mass in a breast we wish to learn whether there is fat atrophy over the lump; whether there is skin dimpling on displacing the breast; its consistency; whether it is cystic and whether it shades off into normal

breast tissue or is sharply marked off from the surrounding breast. If the examiner has these points consecutively in mind and decides each in its turn then the necessary handling can be reduced to a minimum. It is not just to the patient to have students palpate a breast cancer. More of these poor women will survive if the class practices palpation on benign breast tumors.

The practical application of these principles starts when a woman with a lump in her breast presents herself for examination. Let the examining hands touching the questionable lesion be as few and gentle as possible. At operation the field is sterilized with the utmost gentleness. The operation is done by sharp dissection. Gentleness is our aim. Blunt dissection or gauze wiping is avoided entirely. Hemostasis is absolute. It would be interesting to see how many more 5 year cures would result if such methods were universally followed.

HARRY G. SLOAN.

MEMOIRS

C. JEFF MILLER

ON March 21, 1936, America lost one of her most distinguished surgeons and magnetic personalities in the death of Dr. C. Jeff Miller. Dr. Miller, a true son of the South, represented the ultimate in medicine, the science of which was greatly benefited because of his having lived. In addition to his professional attainments probably no physician ever meant as much to a community, either locally or regionally, in a non-professional way than Dr. Miller. His intense interest in the welfare of humanity is illustrated by the fact that he repeatedly took time from his busy teaching and clinical activities to head Community Chest Drives and other similar movements. Not only was his surgical judgment unsurpassed, but also his broad vision and keen insight made his presence on many lay boards of inestimable value.

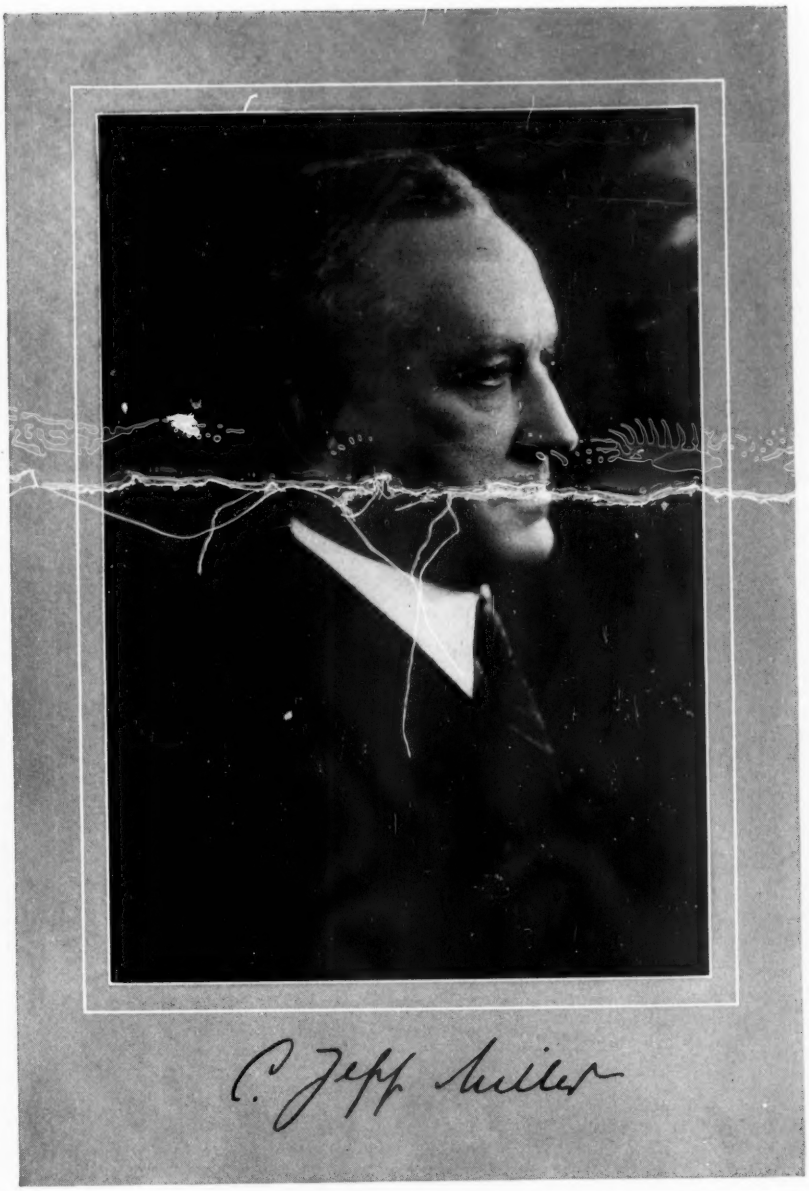
Dr. Miller's education was that of the greatest scholar, as, in addition to his profound knowledge of medicine, he was a connoisseur of music, literature, and art. Some of his happiest hours were spent in his library engrossed in J. M. Barrie, Robert Burns, Osler, and Moynihan.

As a teacher he was unsurpassed, primarily because of his profound knowledge of the subject and also because of his lucid and superb presentations. Even during the most trying operative procedures he lectured clearly, and his operative clinics were always filled to their maximum capacity.

His ability as an executive is exemplified by the organization of his own departments and the great influence he exerted on the many boards on which he served. Often after many hours of heated controversy in which he took no part the question would be quickly settled by his logical deductions.

Those who knew Dr. Miller could understand the devotion of his patients with whom he shared so freely his wise and generous counsel. He always imparted comfort and reassurance to patient and family in the soft tones of his modulated voice.

Dr. Miller was born on February 9, 1874, in Winchester, Tennessee, the son of Charles J. and Elizabeth Johnston Miller. He attended and was graduated from the University of the South, Sewanee, Tennessee. His early ambition to study medicine was undoubtedly kindled during his stay with his uncle, Thaddeus Johnston, a country physician. He received his M.D. degree from the University



C. Jeff Miller

UNIV. OF MICH.

of Tennessee in 1893 and interned at the Nashville City Hospital in 1894. On January 30, 1896, he married Ada Parker, of Memphis, Tennessee, and in 1912 their only daughter, Elizabeth, was born. From 1899 to 1904 he served as chief of clinics at the Charity Hospital, New Orleans, under Dr. Ernest S. Lewis. In 1911 Dr. Miller became professor of gynecology at Tulane University, which position he held until his death. He was chief of the Gynecological Services at the Charity Hospital and Touro Infirmary, New Orleans.

Dr. Miller was officer of many organizations. He served both as secretary and as president of the Orleans Parish Medical Society. From 1926 to 1936 he was a member of the Board of Regents of the American College of Surgeons and was president in 1930–1931; in 1912 he was chairman of the Section on Obstetrics, Gynecology, and Abdominal Surgery of the American Medical Association; president of the Gynecological Club in 1927; president, American Gynecological Society, 1928–1929; president of the Southern Surgical Association in 1922; president of the Southeastern Surgical Congress in 1936; and president of the Howard Memorial Library, New Orleans. During the World War Dr. Miller was a Major in the Medical Corps.

In June, 1930, he received the honorary degree of Doctor of Science from his Alma Mater, Sewanee. He was author of two textbooks, *An Introduction to Gynecology* and *Clinical Gynecology* as well as of innumerable articles on scientific subjects.

Dr. Miller was truly a Southern gentleman and in every way typified Jeffersonian principles. He had the pioneering instinct of Lister, the judgment of Solomon, the technique of Halsted, the tenderness of Florence Nightingale, the perceptive powers of Osler, the determination of Noguchi, and practiced the ethics of Hippocrates.

ALTON OCHSNER.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE small volume by Woods[1] of less than 200 pages is designed to strike a happy medium between what a specialist should know and what is essential to the general practitioner in handling the average run of otitic problems. Consequently, long treatises on otologic problems and detailed anatomical description are purposely omitted.

The illustrations are mostly drawn from life, and on the whole are very good reproductions of pathological conditions.

Having in mind the various problems confronting the general practitioner, the text is practically limited to pyogenic manifestations, and no mention is made of deafness or other otologic problems. There is a good chapter on differential diagnosis of intracranial complication.

The book undoubtedly will be found useful to men in general practice and to medical students.

J. F. DELPH.

A Glasgow Manual of Obstetrics[2], edited by S. J. Cameron, is the second edition of this work, the first having been published in 1924. It is, on the whole, an excellent compilation. An increasing number of teachers and students believe that less padding would improve textbooks. To them the 600 pages of this manual will be a case in point. Except for a rare exception, the illustrations are all line drawings.

The text is completely up to date. The chapter on ovarian and pituitary hormones, though it is short, treats the subject fully and accurately. The discussion of anesthesia considers separately drugs which alleviate pain but do not produce unconsciousness, those which produce only an amnesia, and those which result in complete unconsciousness. The use of chloroform put up in 20 minim perles which can be crushed in a handkerchief for the relief of second stage pain is a suggestion worthy of trial on patients delivered in their homes in this country.

Inasmuch as this manual represents the practice of those associated with the Royal Maternity of Glasgow, it may be well to point out that many of their practices are quite out of favor in this country. This may be accounted for in a measure by their large percentage of home deliveries. Nevertheless the treatment of placenta previa by plugging the vagina with wet cotton pledgets has few supporters here, though it is only fair to say that the authors recommend cesarean section whenever there is no contra-indication. Likewise the removal of the placenta in cases of advanced abdominal pregnancy is rather generally frowned on in this country because of the frequency of uncontrollable hemorrhage. Nor do we feel justified in the use of the hot intrauterine douche for the control of postpartum hemorrhage. The use of sweats in the treatment of pre-eclamptic toxemia has very little acceptance here. The authors are to be commended for their advocacy of prompt emptying of the uterus in any form of toxemia which does not respond rapidly to other treatment.

It is unfortunate that this book will not be widely accepted in this country because of the failure of the English speaking peoples to agree on a common nomenclature for scientific work.

J. E. FITZGERALD.

THE unique book[3] by Harrison differs from most X-ray texts in that it is essentially a clinical presentation, taking up the human body by systems, and giving a discussion of both the diagnostic and therapeutic phases of roentgenology in relation to each. The illustrations are excellent and adequate, considering that the author has limited himself to a single volume.

Special stress is laid upon the need of close association between the radiologist and the referring physician. The utmost information can be obtained from the roentgen study only when the utmost information regarding the suspected pathological condition is considered in planning the examination. Every roentgenological examination is an attempt to solve a definite clinical pathological problem. It should not be undertaken as a foraging expedition. Roentgen investigation is a clinical procedure and roentgen therapy is a clinical treatment. They differ essentially from laboratory tests which are concerned primarily with the examination or treatment of something which is no longer an integral part of the patient. The co-operation between the clinician and the roentgenologist must be sufficiently close to ensure that the patient receives the utmost benefit from the examination. If the information supplied by the clinician is vague and incomplete,

[1] OXFORD MEDICAL PUBLICATIONS. PAINFUL AND DANGEROUS DISEASES OF THE EAR; A TEXT-BOOK FOR STUDENTS AND GENERAL PRACTITIONERS. By R. R. Woods, M.B., F.R.C.S.I. London: Oxford University Press, 1936.

[2] A GLASGOW MANUAL OF OBSTETRICS. By Samuel J. Cameron, M.B., F.R.F.P.S., F.C.O.G., John Hewitt, M.B., Ch.B., F.C.O.G., Robert A. Lennie, M.D., F.R.F.P.S., F.C.O.G., Ellen D. Morton, M.B., Ch.B., M.C.O.G. 2d ed. London: Edward Arnold & Co., 1936.

[3] A TEXTBOOK OF ROENTGENOLOGY; THE ROENTGEN RAY IN DIAGNOSIS AND TREATMENT. By Bede J. Michael Harrison, M.B., Ch.M., D.M.R.E. (Cantab.), F.A.C.R. Baltimore: William Wood & Co., 1936.

the analysis of the roentgenological findings made by the roentgenologist must also be vague and incomplete, and to enable the patient to obtain the best possible advice indefiniteness must be replaced by accuracy. These are principles which the author has set forth in the introduction to his work and they have served as a guide to him consistently throughout the entire book. It deserves a wide circulation and close study. JAMES T. CASE.

ALTHOUGH only a year has passed since the publication of the first edition of *The Radiology of Bones and Joints*[1], Brailsford presents the second edition in which supplementary material has been added. Certain chapters, e.g., those dealing with osteochondritis, bone dystrophies, and spondylolisthesis, have been rewritten. A chapter dealing with dental radiography has been included.

The volume is divided into two parts: (1) "Regional Radiography," and (2) "General Discussion on Bone Changes in Systematic and Localized Disease." Due to the fact that the findings are considered regionally, there are of necessity repetitions of material covering certain bone conditions. The subject matter is well illustrated. Throughout the volume are found frequent references to monographs and articles dealing with the particular condition under discussion. The bibliography at the end of the volume covers 18 pages.

The material covered in the volume of 571 pages includes the rare as well as the more common acquired and congenital bone conditions. The author's discussions of the various conditions are concise but cover the essential roentgen findings.

Part II, covering 83 pages, consists of a general discussion of bone changes in systematic and localized disease. The author draws freely from the available literature.

The volume should prove to be a valuable addition to the reference library not only of the radiologist and surgeon, but also the general practitioner who does not claim to be a specialist but who often encounters unusual, puzzling bone conditions.

EARL E. BARTH.

IN his book, *A Textbook of Obstetrics*[2], Dr. Irving seems to have made a definite step toward the simplification of obstetrical teaching. In the introduction, he states that the book is "designed as a simple and concise textbook for students and practitioners." Furthermore this textbook is an outgrowth from the notes and outlines which have been used for obstetrical teaching in Dr. Irving's department for several years.

There are certain fundamentals in obstetrics that are rather definitely and generally agreed upon by those who are teaching and (or) specializing in this art. This applies chiefly to normal obstetrics; i.e., anatomy and physiology of the reproductive organs both in the pregnant and non-pregnant state. There are certain other phases of the female organism in which our knowledge is much more limited and in which there is considerable diversity of opinion and interpretation. Endocrinology is the number one of this category. Therefore, any statements contained in a textbook on this phase of the subject may have to be revised a year hence. Dr. Irving has presented an excellent résumé of this subject in its relation to the physiology of the female reproductive function, without speculation.

In the matter of pathological obstetrics we are more likely to encounter a greater diversity of opinion among those engaged in its teaching. The difference is usually that of method of treatment of a given condition, and for the most part is relatively unimportant. In this part of the book, a conservative attitude is maintained throughout.

The book is well illustrated and a bibliography at the end of each chapter will be helpful to anyone who wishes to do more extensive reading on that particular subject. There are only 550 pages in this volume which makes the book of practical size for student's use. The contents are arranged in logical order, and one finds it easy reading, clear and concise. CHESTER C. DOHERTY.

THE book by Shelling[3] on the parathyroids in health and disease is an excellent monograph. The text is filled with references. The chapter on hyperparathyroidism, for instance, is followed by a bibliography and 174 articles; that on hypoparathyroidism by 177. Furthermore, this represents a new review of the literature to date; it is not a revision of an old work.

The normal and pathological anatomy of the parathyroids is adequately presented; there is a good description of the cell types found in the normal and hyperplastic gland. The physiological review is written in the light of the author's own research. The clinical discussion of hypoparathyroidism and hyperparathyroidism occupies about one-half of the book. Mistakes in diagnosis and treatment of calcium deficiency states are explained. In this a tabulation of differential diagnosis is helpful. The therapeutic use of parathyroid hormone is critically analyzed. An appendix gives the mineral and caloric values of test diets to be used in the study of questionable cases.

This monograph will be of value to both the surgeon and the internist in the diagnosis and treatment of parathyroid disease. PAUL STARR.

THE fourth edition of von Jaschke's textbook[4] of obstetrics is dedicated to the late Otto Pankow to whom the author acknowledges his indebtedness for much new material on the biology and pathology

[1] THE RADIOLOGY OF BONES AND JOINTS. By James F. Brailsford, M.D. (B'ham), M.R.C.S. (Eng.). 2d ed. Baltimore: William Wood & Co., 1935.

[2] A TEXTBOOK OF OBSTETRICS; FOR STUDENTS AND PRACTITIONERS. By Frederick C. Irving, A.B., M.D., F.A.C.S. New York: The Macmillan Co., 1936.

[3] THE PARATHYROIDS IN HEALTH AND DISEASE. By David H. Shelling, B.Sc., M.D. St. Louis: The C. V. Mosby Co., 1935.

[4] LEHRBUCH DER GEBURTSHILFE. By Dr. Rud. Th. v. Jaschke. 4th ed. Berlin: Julius Springer, 1935.

of pregnancy. This chapter has been rewritten to include the conception of the hormonal influence in the sex cycle.

The text is primarily didactic and is ample in its scope. It is printed on good paper and is rather profusely illustrated with halftones, diagrams, beautifully colored plates, and unusually clear roentgenograms.

Modern methods of diagnosis and treatment prevail for the most part, but the illustration and description of the monaural stethoscope (p. 94) for the detection of fetal heart tones typify the author's adherence to an outmoded method. The head-piece stethoscope, acclaimed universally in this country for two decades, is not mentioned.

Ample bibliographies are appended, containing, however, chiefly German references; few American authorities are cited.

Although a good book for reference, it will probably be in small demand in this country chiefly because at the present rate of exchange the cost of the unbound volume is $18.00, a price indeed out of proportion to the excellent American and English texts covering the same field. IRVING F. STEIN.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

AMERICAN MARTYRS TO SCIENCE THROUGH THE ROENTGEN RAYS. By Percy Brown, M.D., F.A.C.P., F.A.C.R. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1936.

TIME OF OVULATION IN WOMEN; A STUDY ON THE FERTILE PERIOD IN THE MENSTRUAL CYCLE. By Carl G. Hartman. Baltimore: The Williams & Wilkins Co., 1936.

PARENTERAL THERAPY; A READY REFERENCE MANUAL OF EXTRA-ORAL MEDICATION FOR PHYSICIANS, DENTISTS, PHARMACISTS, CHEMISTS, BIOLOGISTS, NURSES, MEDICAL STUDENTS AND VETERINARIANS. By Walter Forest Dutton, M.D., and George Burt Lake, M.D. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1936.

FOTOGRAFIA DEL ESTOMAGO; SUS APLICACIONES EN EL DIAGNOSTICO DEL CANCER DEL ESTOMAGO. By Dr. Herbert Hofmann. Buenos Aires: Aniceto Lopez, Imp., 1936.

SURGICAL EMERGENCIES IN CHILDREN. By Harold Clifford Edwards, M.S.(Lond.), F.R.C.S.(Eng.). Baltimore: William Wood & Co., 1936.

PHYSIOPATHOLOGIE DES OPÉRATIONS SUR LE FOIE ET LES VAISSEAU HÉPATIQUES; LE MÉCANISME DES ACCIDENTS. By Raoul Garling Palmer. Paris: Librairie E. le François, 1934.

NEUROLOGICAL SURGERY. By Loyal Davis, M.S., M.D., Ph.D., D.Sc. (Hon). Philadelphia: Lea & Febiger, 1936.

THE BALANCED DIET. By Logan Clendening, M.D. New York and London: D. Appleton-Century Co., 1936.

PATHOLOGIE UND KLINIK; IN EINZELDARSTELLUNGEN. Edited by L. Aschoff, H. Elias, H. Eppinger, C. Sternberg, K. F. Wenckebach. Band vii. DER ENDEMISCHE KRETINISMUS. By Prof. Dr. F. de Quervain and Prof. Dr. C. Wegelin. Berlin and Vienna: Julius Springer, 1936.

OBSTETRICAL PRACTICE. By Alfred C. Beck, M.D. Baltimore: The Williams & Wilkins Co., 1935.

HANDBOOK OF SURGERY. By Eric C. Mekie, M.B., Ch.B., F.R.C.S.(Edin.). With a foreword by John Fraser, M.C., M.D., Ch.M., F.R.C.S.E. Baltimore: William Wood & Co., 1936.

EMERGENCY SURGERY. By Hamilton Bailey, F.R.C.S. (Eng.) 2d ed. Baltimore: William Wood & Co., 1936.

THE ADRENALS. By Arthur Grollman, Ph.D., M.D. Baltimore: The Williams & Wilkins Co., 1936.

MEDIZINISCHE PRAXIS; SAMMLUNG FUER AERZTLICHE FORTBILDUNG. Edited by Prof. Dr. L. R. Grote, Prof. Dr. A. Fromme and Prof. Dr. K. Warnekros. Vol. ix—BLUTUNG UND FLUOR. By Prof. Dr. Hans Runge. Dresden and Leipzig: Theodor Steinkopff, 1936.

THE PRACTITIONERS LIBRARY OF MEDICINE AND SURGERY. Vol. x—DERMATOLOGY AND SYPHILOLOGY. New York and London: D. Appleton-Century Co., 1936.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

DONALD C. BALFOUR, Rochester, *President* EUGENE H. POOL, New York, *President-Elect*
HENRY P. BROWN, JR., *Chairman;* GILSON C. ENGEL, *Secretary, Committee on Arrangements*

PRELIMINARY CLINICAL PROGRAM FOR 1936 CLINICAL CONGRESS

FOR the twenty-sixth annual Clinical Congress of the American College of Surgeons to be held in Philadelphia, October 19–23, 1936, the surgeons of that great medical center have organized under the leadership of a strong and representative committee. They plan to provide a program of surgical clinics and demonstrations that will present a complete showing of their clinical activities in all departments of surgery. The committee is assured of the hearty co-operation of the clinicians at the five medical schools and more than thirty hospitals that will participate in the clinical program.

The Executive Committee in charge of arrangements is as follows: Henry P. Brown, Jr., chairman; Gilson C. Engel, secretary; Francis H. Adler, Dorothy C. Blechschmidt, John O. Bower, L. K. Ferguson, Bruce L. Fleming, Karl M. Houser, Robert H. Ivy, H. P. Leopold, Richard H. Meade, Jr., Francesco Mogavero, John R. Moore, E. A. Mullen and Lewis C. Scheffey.

A preliminary schedule of such clinics and demonstrations appears in the following pages. Published in tentative form, and incomplete as to the participating hospitals, the clinical program is to be revised and amplified during the coming months as the work of the program committee progresses. It will be noted that operative clinics and demonstrations in the hospitals are scheduled for the afternoon of Monday, October 19, beginning at 2 o'clock, and for the mornings and afternoons of each of the four following days. The real program of the Congress will be published from day to day—a complete and accurately detailed program being posted in the form of bulletins at headquarters each afternoon for the succeeding day and issued in printed form the following morning. All departments of surgery will be represented therein—general surgery, gynecology and obstetrics, genito-urinary surgery, neurosurgery, orthopedics, surgery of the eye, ear, nose and throat.

The following hospitals will participate in the clinical program: Abington, American Oncologic, Broad Street, Bryn Mawr, Chestnut Hill, Children's, Children's Hospital of the Mary J. Drexel Home, Cooper (Camden), Delaware County, Episcopal, Fitzgerald-Mercy, Frankford, Germantown, Graduate Hospital of the University of Pennsylvania, Hahnemann, Hospital of the University of Pennsylvania, Hospital of Woman's Medical College, Jeanes, Jefferson, Jewish, Kensington, Lankenau, Memorial, Methodist Episcopal, Misericordia, Mount Sinai, Northeastern, Pennsylvania, Philadelphia General, Philadelphia Orthopædic, Presbyterian, St. Agnes, St. Christopher's, St. Joseph's, St. Luke's and Children's, St. Mary's, St. Vincent's, Shriner's, Stetson, Temple University, Wills Eye, Woman's.

The committee is planning to develop many special features in the clinical program including among other features: (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray; (2) fracture clinics demonstrating modern methods in the treatment of fractures; (3) clinics in traumatic surgery for the presentation of the newer methods of rehabilitation of the injured by surgery and physical therapy.

In addition to an extensive schedule of operative clinics and demonstrations at the hospitals, the subcommittee on ophthalmology and otolaryngology is preparing a series of clinical demonstrations to be given by visiting ophthalmologists and otolaryngologists, to be presented each forenoon at the headquarters hotel.

EVENING MEETINGS

Programs for the five evening scientific sessions, to be held in Irvine Hall, are being prepared by

the Executive Committee of the Board of Regents. At the presidential meeting on Monday evening, the first formal session of the Congress, the retiring president, Dr. Donald C. Balfour, will deliver his address. At this session the new officers will be inaugurated: Dr. Eugene H. Pool, New York, president; Dr. Emile Holman, San Francisco, first vice-president; Dr. George E. Wilson, Toronto, second vice-president.

At the annual Convocation of the College on Friday evening the 1936 class of initiates will be received into Fellowship. On this occasion Dr. Eugene H. Pool will deliver the presidential address. At sessions on Tuesday, Wednesday and Thursday evenings eminent surgeons of the United States and Canada, together with a number of visiting surgeons from foreign countries, will present and discuss papers dealing with surgical subjects of timely importance.

It is expected that at this year's Congress we will be honored by the presence of a number of distinguished European surgeons. Among those who have indicated that they will attend are the following: Sir James Walton, London, England; Dr. William Fletcher Shaw, Manchester, England; Archibald Hector McIndoe, London, England; Dr. Alexander MacLennan, Glasgow, Scotland; Prof. Dr. Paul Clairmont, Zurich, Switzerland; Prof. Dr. Martin Kirschner, Heidelberg, Germany; Prof. Wolfgang Rosenthal, Leipzig, Germany; and Prof. Dr. F. Sauerbruch, Berlin, Germany.

SPECIAL FEATURES OF THE PROGRAM

Special features of the program for this year's Congress include: (1) A conference on fractures under the auspices of the Committee on the Treatment of Fractures; (2) a symposium on cancer arranged by the Committee on the Treatment of Malignant Diseases, (3) a conference on industrial medicine and traumatic surgery under the auspices of the Committee on Industrial Medicine and Traumatic Surgery.

The showing of surgical motion pictures, demonstrating clinical features of interest, has met with popular acceptance in recent years and will be continued at this year's Congress with an enlarged program of films, both sound and silent, to be exhibited daily at headquarters.

Following its established custom and in recognition of an obligation to the public to provide authoritative information on modern surgery, better hospitals and the prevention of disease, a community health meeting will be held on Wednesday evening under the auspices of the College in the Municipal Auditorium.

HOSPITAL CONFERENCE

The annual hospital conference will open the Congress with a session in the Rose Garden of the Bellevue-Stratford Hotel at 10 o'clock on Monday morning. An interesting program of papers, round table conferences, and practical demonstrations dealing with problems related to hospital efficiency is being prepared for sessions on Monday, Tuesday, Wednesday and Thursday. A greatly increased interest on the part of surgeons in both the administrative and scientific phases of hospital work has been evidenced in recent years and the program for this year's conference will provide for discussions of subjects of interest to the three major hospital groups—medical, surgical, and administrative. It is proposed to make this year's program of wide interest and practical character through a careful selection of subjects to be presented and discussed by surgeons and hospital executives, particular emphasis being directed toward professional standards and the vital problems related to hospital economics.

HEADQUARTERS—TECHNICAL EXHIBITION

Clinical Congress headquarters will be established at the Bellevue-Stratford Hotel, which has unusual facilities for accommodating the Congress. The grand ballroom, Garden, Clover and Red Rooms and other large rooms on the first and second floors and the roof have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, executive offices, etc. Thus, the activities of the Congress will be centralized under one roof.

The Technical Exhibition will be located in the ballroom and adjacent large rooms on the second floor. The registration and clinic ticket bureau together with the registration desk will be centrally located as regards the exhibit rooms, in which will be placed the bulletin boards on which the daily clinical program will be posted each afternoon. Leading manufacturers of surgical instruments and supplies, X-ray apparatus, operating room lights, hospital apparatus and supplies of all kinds, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this Exhibition.

ADVANCE REGISTRATION

The hospitals and medical schools of Philadelphia afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the

amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of $5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

PHILADELPHIA HOTELS AND THEIR RATES

In addition to the headquarters hotel, the Bellevue-Stratford, there are several first-class hotels within short walking distance of headquarters, providing ample hotel facilities at reasonable rates. It is suggested that reservation of hotel accommodation be made at an early date. The following hotels are recommended by the Committee:

	Minimum Rate with Bath	
	Single	Double
Adelphia, 13th and Chestnut Sts.	$3.50	$5.00
Barclay, Rittenhouse Square, E.	4.00	6.00
Belgravia, 1811 Chestnut St.	2.50	4.00
Bellevue-Stratford, Broad and Walnut Sts.	4.00	6.00
Benjamin Franklin, 9th and Chestnut Sts.	3.50	5.00
Broadwood, Broad and Wood Sts.	2.00	4.00
Colonial, 11th and Spruce Sts.	2.50	3.50
Covington, 37th above Chestnut St.	2.00	3.00
Drake, 1512 Spruce St.	4.00	6.00
Lorraine, Broad St. and Fairmount Ave.	2.50	5.00
Majestic, Broad St. and Girard Ave.	2.50	4.00
Normandie, 36th and Chestnut Sts.	2.50	3.50
Pennsylvania, 39th and Chestnut Sts.	2.50	4.00
Rittenhouse, Chestnut at 22nd St.	2.00	3.50
Ritz Carlton, Broad and Walnut Sts.	3.50	6.00
Robert Morris, 17th and Arch Sts.	2.50	4.00
Roosevelt, 23rd and Walnut Sts.	2.50	4.00
Spruce, 13th and Spruce Sts.	2.00	3.00
St. James, 13th and Walnut Sts.	2.50	4.00
Stephen Girard, 2027 Chestnut St.	2.50	4.00
Sylvania, Juniper and Locust Sts.	3.00	5.00
Walton, Broad and Locust Sts.	2.50	4.00
Warwick, 17th and Locust Sts.	4.00	6.00
Wellington, 19th and Walnut Sts.	4.00	5.00

PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY, NEUROSURGERY, SURGICAL PATHOLOGY, ETC.

JEFFERSON HOSPITAL

Monday

ROSS V. PATTERSON—2. The use of drugs in surgical cases.
WILLIS F. MANGES—3. Treatment of acute infection by X-ray.

Tuesday

VIRGIL H. MOON—9. Shock: Its mechanism, pathology and sequellæ, illustrated.
GEORGE A. ULRICH and staff—9. Obstetrical operations.
DAVID M. DAVIS—9. Urological operations.
ARTHUR FIRST—9:30. Sterility clinic.
J. TORRANCE RUGH—10. Orthopedic operations.
P. BROOKE BLAND and staff—9. Obstetrical and gynecological operations.
CHARLES F. NASSAU—11. General surgery and ward walks.
JAMES CARRELL—12. Ward walks.
RANDALL MACCARROLL—12. Antenatal clinic.
JOHN MONTGOMERY and CHARLES LINTGEN—12. Post-operative follow-up clinic.
P. BROOKE BLAND and staff—1:30. Antenatal clinic, demonstrations in laboratory, clinical study of sterility, parasitic infestations of vagina.
EDWARD J. KLOPP—2. General surgery.

Wednesday

BROOKE M. ANSPACH, JOHN B. MONTGOMERY and staff—9. Gynecological operations.
WARREN B. DAVIS—9. Plastic and oral surgery.
HARRY STUCKERT and staff—9:30. Gynecological and obstetrical operations.
P. BROOKE BLAND and staff—9. Obstetrical and gynecological operations.
DAVID M. DAVIS—10. Urological operations, demonstration of cases.
H. M. GINSBERG—10:30. Cystoscopic clinic.
ARTHUR E. BILLINGS—11. General surgery and ward walks.
EDWARD L. BAUER—12. Diagnosis and treatment of pylorospasm and obstruction by congenital duodenal bands, ward walk.
JOHN DUGGER—12. Antenatal clinic.
T. L. MONTGOMERY—12. Ward walks.
P. BROOKE BLAND and staff—1:30. Antenatal clinic, demonstrations in laboratory, clinical study of sterility, parasitic infestations of vagina.
T. A. SHALLOW—2. General surgery.
MARIO CASTALLO—2. Treatment of venereal diseases in antenatal period, demonstration and presentation of cases.

Thursday

LEWIS C. SCHEFFEY, CHARLES LINTGEN and staff—9. Gynecological operations.
WARREN B. DAVIS—9. Plastic and oral surgery.
T. L. MONTGOMERY and staff—9. Obstetrical and gynecological operations.
P. BROOKE BLAND and staff—9. Obstetrical and gynecological operations.
DAVID M. DAVIS—10. Urological operations.
HENRY K. SEELAUS and P. A. MCCARTHY—11. General surgery and ward walks.
P. BROOKE BLAND and staff—1:30. Antenatal clinic, demonstrations in laboratory, clinical study of sterility, parasitic infestations of vagina.
E. J. KLOPP, W. F. MANGES, F. C. KNOWLES, B. L. CRAWFORD and W. H. KRAEMER—3. Tumor clinic conference.
BROOKE M. ANSPACH and LEWIS C. SCHEFFEY—3. Clinical conference in gynecology.
P. BROOKE BLAND—4. Obstetrical conference.
T. L. MONTGOMERY and J. BERNARD BERNSTEIN—4. Manikin instruction.

Friday

WARREN B. DAVIS—9. Plastic surgery operations.
GEORGE A. ULRICH and JAMES CARRELL—9. Obstetrical and gynecological operations.
DAVID M. DAVIS—9. Urological operations.
P. BROOKE BLAND and staff—10. Obstetrical operations.
MICHAEL A. BURNS—10. Brain tumors.
JOHN B. FLICK—11. General surgery and ward walks.
LEWIS C. SCHEFFEY and W. J. THUDIUM—12. Uterine carcinoma, follow-up clinic.
JACOB HOFFMAN—12. Endocrinological clinic.
JAMES CARRELL—12. Ward walks.
JOHN DUGGAR—12. Antenatal clinic.
ARTHUR FIRST and REGINA HOBAN—2. Biological studies in pregnancy.

HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Monday

Staff—2. Pre- and postoperative care of surgical cases, demonstrations in the Laboratory of Surgical Research.

Tuesday

I. S. RAVDIN and staff—9. General surgical operations.
C. C. NORRIS and staff—9. Gynecological operations.
A. RANDALL—2. Urological operations.
Staff—2. Demonstrations in the Laboratory of Surgical Research.

Wednesday

E. L. ELIASON and staff—9. General surgical operations.
C. C. NORRIS and C. BACHMAN—9. Obstetrical clinic.
Staff—2. Pre- and postoperative care of surgical cases.
BRUCE GILL—2. Orthopedic clinic.

Thursday

I. S. RAVDIN and staff—9. General surgical operations.
F. E. KEENE—9. Gynecological operations.
BRUCE GILL—2. Orthopedic operations.
A. RANDALL—2. Urological operations.

Friday

E. L. ELIASON and staff—9. General surgical operations.
Staff—9. Obstetrical clinic.
C. C. NORRIS and staff—2. Gynecological operations.

EVANS INSTITUTE

Wednesday

R. H. IVY and LAURENCE CURTIS—10. Oral surgery.

TEMPLE UNIVERSITY HOSPITAL

Monday

W. EDWARD CHAMBERLAIN—1. Demonstration of biplane fluoroscope especially adapted for bronchoscopy.
W. EDWARD CHAMBERLAIN, CHARLES L. BROWN, W. EMORY BURNETT, CHEVALIER L. JACKSON, LOUIS COHEN and ROBERT F. RIDPATH—3. Chest conference.
LAWRENCE W. SMITH—3. Surgical pathological conference.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—4. Hydrodynamics of the craniovertebral cavity, working model.

Tuesday

W. WAYNE BABCOCK—9. General surgical clinic.
TEMPLE FAY—9. Neurosurgical operations.
JOHN FRICK—9. General surgical clinic.
LOUIS COHEN—10. Artificial pneumothorax, ambulant cases.
J. O. ARNOLD—11. Intradermal test for pregnancy.
JOHN O. BOWER and staff—11. Surgical research laboratory.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—11. Hydrodynamics of the craniovertebral cavity, working model.
W. EMORY BURNETT—1. Diseases of the breast.
JOHN R. MOORE—2. Fractures, deliberate delayed reduction.
W. HERSEY THOMAS—3. Genito-urinary clinic.
FRANK W. KONZELMANN—3. Surgical pathological conference.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—4. Hydrodynamics of the craniovertebral cavity, working model.

Wednesday

W. WAYNE BABCOCK—9. General surgical clinic.
J. NORMAN COOMBS—9. General surgical clinic.
TEMPLE FAY—9. Conference on neurological and neurosurgical problems, ward rounds.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—11. Hydrodynamics of the craniovertebral cavity, working model.
W. EMORY BURNETT—12. Plastic surgery clinic.
W. WAYNE BABCOCK and CHARLES L. BROWN—1. Surgical medical conference.
TEMPLE FAY—2. Fractures of skull and cerebral trauma.
HARRY Z. HIBSHMAN and staff—3. Proctological operations.
LAWRENCE W. SMITH—3. Surgical pathological conference.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—4. Hydrodynamics of the craniovertebral cavity, working model.

Thursday

W. WAYNE BABCOCK—9. General surgical clinic.
JOHN LEEDOM—9. General surgical clinic.
TEMPLE FAY—9. Neurosurgical operations, relief of pain.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—11. Hydrodynamics of craniovertebral cavity, working model.
JOHN O. BOWER and staff—11. Surgical research laboratory.
W. EMORY BURNETT—12. Thoracic surgery clinic.
TEMPLE FAY—1. Management of convulsive seizures, epilepsy.
W. EDWARD CHAMBERLAIN—1. Biplane fluoroscope especially adapted for bronchoscopy.
J. O. ARNOLD—2. Toxemia clinic: Demonstration of fluid balance, methods, case records and results.
JOHN R. MOORE—2. Orthopedic clinic: Spine, angle point fusion; shoulder, posterior glenoid repair for luxation; hip, shelf procedure for shallow socket.
W. HERSEY THOMAS—3. Genito-urinary clinic.
FRANK W. KONZELMANN—3. Surgical pathological conference.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—4. Hydrodynamics of craniovertebral cavity, working model.

Friday

W. WAYNE BABCOCK—9. General surgery.
W. EMORY BURNETT—9. General surgical clinic.
TEMPLE FAY—9. Headache, its mechanism and methods of treatment.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—11. Hydrodynamics of craniovertebral cavity, working model.
JESSE O. ARNOLD and staff—11. Obstetrical operations.
JOHN O. BOWER and staff—11. Surgical research laboratory.
FRANK C. HAMMOND—12. Gynecological clinic.
CHARLES L. BROWN—1. Cardiac patients as surgical risks.
TEMPLE FAY—2. Control of intracranial pressure by methods of dehydration.
W. EDWARD CHAMBERLAIN, CHARLES L. BROWN, W. EMORY BURNETT, CHEVALIER L. JACKSON, LOUIS COHEN and ROBERT F. RIDPATH—3. Chest conference.
LAWRENCE W. SMITH—3. Surgical pathological conference.
W. EDWARD CHAMBERLAIN and TEMPLE FAY—4. Hydrodynamics of craniovertebral cavity, working model.

METHODIST EPISCOPAL HOSPITAL

Tuesday

CALVIN SMYTH and staff—9. General surgical operations.
GEORGE J. SCHWARTZ and staff—9. General surgical operations.

Wednesday

CALVIN SMYTH and staff—9. General surgical operations.
GEORGE J. SCHWARTZ and staff—9. General surgery.
ROY W. MOHLER—9. Cesarean section; Fothergill-Manchester operation for uterine prolapse.
STERLING MOORHEAD—2. Urological operations.

Thursday

ROY W. MOHLER—10:30. Prenatal clinic.

ST. MARY'S HOSPITAL

Tuesday

LEO WOJCZYNSKI—11. Uterine cancer.

Wednesday

J. M. LAFERTY—9. Obstetrical clinic.
JOSEPH TOLAND—11. Pelvic infections, operative and nonoperative.

Thursday

WILLIAM F. MORRISON—11. Perineal repair, including complete tears.

CHILDREN'S HOSPITAL OF DREXEL HOME

Days to be announced

ALBERT C. MARTIN. Fluid balance in postoperative treatment.
JOHN HAND. Fractures in children.
J. ALBRIGHT JONES. Abdominal pain in children. Discussed by ELIZABETH KIRK ROSE.
J. MONTGOMERY DEAVER. Appendicitis in childhood.
GILSON C. ENGEL. The treatment and results of hernia in children.

ST. JOSEPH'S HOSPITAL

Tuesday and Thursday

F. HURST MAIER—10. The value of the Fothergill operation in the treatment of uterine prolapse.

PHILADELPHIA GENERAL HOSPITAL

Monday

H. R. OWEN—1:30. General surgical operations.

Tuesday

WILLIAM F. MOORE—9. Treatment of bronchiectasis and pulmonary suppuration.
HENRY S. RUTH and staff—9. Cyclopropane in thoracic surgery.
L. D. ENGLERTH—9. General surgical operations.
M. P. WARMUTH—9. General surgical operations.
C. A. BEHNEY—10. Treatment of gynecological cancer.
I. S. HNELESKI—11. Preparation of intravenous solutions and trays, demonstration.
RICHARD MEADE—11. Management of pulmonary tuberculosis by means of artificial pneumothorax and allied operatons.
EDWARD A. SCHUMANN and staff—1. Gynecological clinic.
MOSES BEHREND—2. Thoracic surgery.

Wednesday

HENRY S. RUTH and staff—9. Trends in anesthetic methods at Philadelphia General Hospital.
P. A. MCCARTHY and associates—9. General surgical operations.
JOHN BOWER and associates—9. Treatment of spreading peritonitis complicating acute perforative appendicitis; use of convalescent serum and perfringes antitoxin.
I. S. HNELESKI—11. Preparation of intravenous solutions and trays, demonstration.
L. H. CLERF—1. Diagnosis and treatment procedures for intra-oral cancer.
W. G. ELMER and L. D. FRESCOLN—3. Fractured hips.

Thursday

TEMPLE FAY—9. Neurosurgery.
HENRY S. RUTH and staff—9. Choice of anesthetic agents and methods.
L. D. ENGLERTH—9. General surgical operations.
M. P. WARMUTH—9. General surgical operations.
J. C. HOWELL—9. Breast cancer.
I. S. HNELESKI—11. Preparation of intravenous solutions and trays, demonstration.
JOSEPH MACFARLAND and staff—1. Tumor clinic—general discussion of management, treatment and diagnosis of various types of malignant diseases.
W. H. MACKINNEY—2. Urological operations, demonstration of cases.
JOHN D. REESE—2. Plastic and oral surgery.

Friday

J. C. HOWELL—9. Cancer operations.
P. A. MACCARTHY and associates—9. General surgical operations.
HENRY S. RUTH and staff—9. Pre-anesthetic sedation.
I. S. HNELESKI—11. Preparation of intravenous solutions and trays, demonstration.
B. P. WIDMANN—2. Technical procedures of X-ray and radium therapy.

STETSON HOSPITAL

Wednesday

STEPHEN E. TRACY—9. Gynecological cases.

Friday

STEPHEN E. TRACY—9. Gynecological cases.

EPISCOPAL HOSPITAL

Tuesday

I. M. BOYKIN, J. W. KLOPP and R. R. LAYTON—9. General surgery.
I. M. BOYKIN—12. Dry clinic: Amputations for diabetic gangrene.

Wednesday

H. E. KNOX—9. Surgical management of pyloric and duodenal obstruction in infants.
R. H. MEADE, JR.—9. Factors influencing late results in treatment of acute perforation of peptic ulcers.
LOWRY ALLEN—9. X-ray treatment of acute surgical infections.
E. T. CROSSAN—9. The management of acute osteomyelitis.
JOHN KLOPP and R. R. LAYTON—9. The management of fractures about the ankle.
RUTHERFORD L. JOHN—2. Orthopedic surgery.
ALBERT MARTUCCI—4. The management of peripheral vascular disease.

Thursday

E. T. CROSSAN, H. E. KNOX and R. H. MEADE, JR.—9. General surgery.

Friday

I. M. BOYKIN, J. W. KLOPP and R. R. LAYTON—9. General surgery.

PRESBYTERIAN HOSPITAL

Tuesday

E. B. HODGE, E. L. WILLIAMSON and L. M. RANKIN—9. General surgery.
R. H. IVY and L. CURTIS—9. Maxillofacial surgery.
A. B. GILL and T. E. ORR—1:30. Orthopedic surgery.
G. M. LAWS, J. P. LEWIS, D. RIEGEL and J. F. SCHELL—1:30. Gynecological operations.
C. FOULKROD, P. F. WILLIAMS, W. C. ELY, F. A. MILLER and V. T. SHIPLEY—4. Obstetrical conference.

Wednesday

WILLIAM BATES, J. B. MASON and J. C. HOWELL—9. General surgery.
J. C. BEARDWOOD, F. A. BOTHE and H. T. KELLY—10:30. Surgical aspects of diabetes, abdominal symptoms of diabetes, gangrene prophylaxis.
J. C. BIRDSALL, F. G. HARRISON, S. EARHART and HENRY SANGREE—1:30. Urology, operative and dry clinic.

Thursday

E. L. ELIASON, F. A. BOTHE and J. P. NORTH—9. General surgery.
C. A. BEHNEY and J. C. GRIFFITH—1:30. Gynecology.

Friday

H. P. BROWN, JR. and O. C. KING—9. General surgery.
GEORGE M. LAWS—1. Gynecology.

CHILDREN'S HOSPITAL

Days to be announced

W. E. LEE, DR. ROBBINS and O. KING. General surgery.
ROBERT IVY. Plastic surgery.
JESSE NICHOLSON. Orthopedic surgery.

ST. VINCENT'S HOSPITAL

Wednesday

WILLIAM F. MORRISON—10. Gonorrhea of the female tract with complications.

GRADUATE HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Monday

JOSEPH C. BIRDSALL, L. F. MILLIKEN, F. G. HARRISON and F. ROSENBLUM—2. Genito-urinary surgery, demonstration of cases.

Tuesday

WILLIAM BATES—9. General surgery.
WILLIAM H. MACKINNEY and EDWARD A. MULLEN—2. Genito-urinary surgery.

Wednesday

WILLIAM R. NICHOLSON—9. Gynecological surgery.
WALTER ESTELL LEE and H. L. BOCKUS—9. General surgery.

Thursday

FRANCIS C. GRANT—9. Neurosurgery.
JACOB W. CUTLER—9. Intrapleural pneumolysis.

Friday

ROBERT H. IVY and LAURENCE CURTIS—9. Maxillofacial surgery.
W. E. LEE and C. F. MARTIN—9. Lymphopathia venereum.

PENNSYLVANIA HOSPITAL

Tuesday

NORRIS W. VAUX—9:30. Gynecological and obstetrical operations, demonstration of cases and clinical exhibits.
LEON HERMAN—2. Urological operations, demonstration of cases.

Wednesday

NORRIS W. VAUX—9:30. Gynecological and obstetrical operations, demonstration of cases and clinical exhibits.

Thursday

NORRIS W. VAUX—9:30. Gynecological and obstetrical operations, demonstration of cases and clinical exhibits.

Friday

NORRIS W. VAUX—9:30. Gynecological and obstetrical operations, demonstration of cases and clinical exhibits.

NORTHEASTERN HOSPITAL

Tuesday

T. T. THOMAS—10. Fracture clinic—upper extremities.

Wednesday

FREDERICK E. KELLER and ALFRED H. DIEBEL—9. Gynecological operations.
T. T. THOMAS—10. Fracture clinic—lower extremities.
J. B. LOWNES and HAROLD LIPSHUTZ—2. Genito-urinary clinic.

Thursday

T. T. THOMAS—10. Fracture clinic—upper extremities.
FREDERICK E. KELLER and ALFRED H. DIEBEL—3. Obstetrical clinic, demonstration of cases.

Friday

T. T. THOMAS—10. Fracture clinic—lower extremities.

LANKENAU HOSPITAL

Monday

W. H. MACKINNEY—2. Urological operations.

Tuesday

D. B. PFEIFFER, J. M. DEAVER, CLARK BROWN and EDWARD BORTZ—9. General surgery, operations and demonstration of cases.

Wednesday

G. P. MULLER, G. C. ENGEL, DR. MAY and J. KEEZEL—9. General surgery, operations and demonstrations.

Thursday

D. B. PFEIFFER, J. M. DEAVER, CLARK BROWN and EDWARD BORTZ—9. General surgery, operations and demonstration of cases.

Friday

G. P. MULLER, G. C. ENGEL, DR. MAY and J. KEEZEL—9. General surgery, operations and demonstrations.

WOMAN'S MEDICAL COLLEGE HOSPITAL

Tuesday

J. S. RODMAN and associates—11. General surgery.

Thursday

LIDA STEWART COGILL and CONSTANCE VOLK—9. Postnatal clinic.
HELEN M. ANGELUCCI—9. Treatment of trichomonas vaginalis.
FAITH FETTERMAN—10. Postirradiation lesions of urinary tract.
LIDA STEWART COGILL—11. Ward walks with demonstration of interesting cases.
MARGARET STURGIS and ELEANOR BALPH—11. Sterility clinic: Tubal insufflation and lipiodol injections.
ANN GRAY TAYLOR—1. Prenatal clinic.
CATHERINE MACFARLANE and FAITH FETTERMAN—2. Gynecological operations.
CATHERINE MACFARLANE and VIRGINIA RHEUBY—3:30. Treatment of dysfunctional uterine bleeding.

ST. AGNES HOSPITAL

Monday

W. H. HAINES—12:30. Genito-urinary surgery.

Tuesday

C. C. MURPHY—9. General surgery.
J. A. MCGLINN and W. B. HARER—9. Gynecology.
H. SANGMEISTER, W. SUSSMAN and Y. F. YOSHIDA—9. Obstetrical clinic.

Wednesday

J. W. BRANSFIELD—9. General surgery.
G. M. DORRANCE—9. Plastic surgery.
L. AVERETT and W. SUSSMAN—9. Gynecology.
H. SANGMEISTER, W. B. HARER and Y. F. YOSHIDA—9. Obstetrical clinic.
W. H. HAINES—2. Genito-urinary surgery.

Thursday

A. P. KEEGAN—9. General surgery.
J. A. MCGLINN—9. Gynecology.
H. SANGMEISTER, W. B. HARER, W. SUSSMAN and Y. F. YOSHIDA—9. Obstetrical clinic.

Friday

G. M. DORRANCE and J. W. BRANSFIELD—9. General surgery.
J. A. MCGLINN and L. AVERETT—9. Gynecology.

AMERICAN ONCOLOGIC HOSPITAL

Tuesday

GEORGE M. DORRANCE—12. Conference on neoplastic diseases.
GEORGE M. DORRANCE—2. Plastic surgery and surgery of malignancy.

Wednesday

GEORGE M. DORRANCE—12. Conference on neoplastic diseases.

Thursday

STEPHEN E. TRACY—9. Carcinoma of uterus.
GEORGE M. DORRANCE—12. Conference on neoplastic diseases.
GEORGE M. DORRANCE—2. Plastic surgery and surgery of malignancy.

Friday

GEORGE M. DORRANCE—12. Conference on neoplastic diseases.

MOUNT SINAI HOSPITAL

Monday

M. BEHREND—1:15. General surgical operations.

Tuesday

E. L. ELIASON—9. General surgical operations.
B. LIPSHUTZ—9. General surgical operations.
M. MUSCHAT—1:30. Urological operations.

Wednesday

C. MAZER—9. Gynecological operations.
M. COOPERMAN—2. Orthopedic surgery.

Thursday

B. MANN—9. Gynecological operations.
M. MUSCHAT—1:30. Urological surgery.

Friday

B. LIPSHUTZ—9. General surgical operations.
M. BEHREND—1:15. General surgery.

GERMANTOWN HOSPITAL

Tuesday

E. B. HODGE, W. B. SWARTLEY, S. D. WEEDER and R. S. ALSTON—10:30. General surgical clinic.
DR. MCLAUGHLIN and S. S. WOOLSTON—1:30. Varicose vein clinic.

Wednesday

STANLEY Q. WEST—9. Urological operations.
C. F. MITCHELL, W. E. LEE, H. E. KNOX and T. M. DOWNS—9:30. General surgical clinic.
W. E. LEE and T. M. DOWNS—2. Thoracic surgery.

WOMEN'S HOMEOPATHIC HOSPITAL

Tuesday and Friday

B. F. BISCOE and F. L. HUGHES—9. Gynecology and obstetrics.

ST. CHRISTOPHER'S HOSPITAL

Wednesday

HARRY E. KNOX, JOHN WOLF and L. M. EBLE. Surgery of childhood.

SHRINERS' HOSPITAL

Days to be announced

JOHN R. MOORE. Orthopedic surgery.

COOPER HOSPITAL
(Camden, N. J.)

Tuesday

B. F. BUZBY and DR. CARLANDER—9. Orthopedic operations.
T. B. LEE and G. F. WEST—9. Gynecological operations.
P. M. MECRAY, A. S. ROSS, F. W. SHAFER and I. E. DEIBERT—10. General surgery.
R. S. GAMON—10. Fracture clinic and demonstration of cases.
A. B. DAVIS, J. HARRIS UNDERWOOD, LAWRENCE GLOVER and GEORGE B. GERMAN—11:30. Prenatal clinic, demonstration of obstetrical cases.
A. H. LIPPINCOTT, D. F. BENTLEY, JR. and R. R. BETANCOURT—2. Urology.

Wednesday

P. M. MECRAY, A. S. ROSS, F. W. SHAFER and I. E. DEIBERT—9. General surgery.
A. B. DAVIS and staff—9. Obstetrical clinic.

Thursday

B. F. BUZBY and DR. CARLANDER—8. Orthopedic operations.
T. B. LEE and G. F. WEST—9. Gynecological operations.
P. M. MECRAY and staff—10. General surgery.
A. B. DAVIS, J. HARRIS UNDERWOOD, LAWRENCE GLOVER and GEORGE B. GERMAN—11:30. Prenatal clinic, demonstration of obstetrical cases.
A. B. DAVIS—2. Obstetrical operations.

Friday

Staff—9. General surgery, operative and dry clinic.

JEWISH HOSPITAL

Tuesday

J. B. LOWNES—9. Urological operations.
M. BEHREND—9. General surgery.
W. H. TELLER—2. General surgery.

Wednesday

F. B. BLOCK—9. General surgery.
M. BEHREND—2. General surgery.

Thursday

C. J. STAMM—9. Gynecology and obstetrics.
F. B. BLOCK—2. General surgery.

Friday

R. GOLDSMITH—9. General surgery.
F. F. WILLIAMS, C. J. STAMM, J. WALKER and F. C. HAMMOND—9. Obstetrical and gynecological clinic.
W. H. TELLER—2. General surgery.

BRYN MAWR HOSPITAL

Tuesday

A. BILLINGS and staff—10. General surgery.

Wednesday

W. E. LEE and staff—2. General surgery.

Thursday

J. S. RODMAN and staff—10. General surgery.
LEON HERMAN—2. Urological operations.

KENSINGTON HOSPITAL

Days to be announced

A. E. PARKE, A. D. VOGELEIN, J. H. MISSETT, JR., SAMUEL STERN, Z. B. NEWTON and F. J. KOWNACKI. Gynecological and obstetrical clinics.

MISERICORDIA HOSPITAL

Tuesday

B. R. Beltran and E. J. Garvin—9. General surgery, operative and dry clinic.
G. P. Muller, F. Mogavero and F. T. McGinnis—9. General surgery, operative and dry clinic.
J. A. Sharkey—10. Planned obstetrical admissions and their influence upon obstetrical mortality and morbidity.

Wednesday

J. A. Kelly and D. C. Geist—9. General surgery, operative and dry clinic.
T. J. Ryan, J. F. Dougherty and J. B. Claffey—9. General surgery, operative and dry clinic.
F. A. Loeffflad—10. Varicose vein clinic.
A. Kurtz—11. Orthopedic clinic.
W. J. MacMurtrie—2. Toxemias of pregnancy.

Thursday

G. P. Muller, F. Mogavero and F. T. McGinnis—9. General surgery, operative and dry clinic.
B. R. Beltran and E. J. Garvin—9. General surgery, operative and dry clinic.
J. V. Missett—2. Reduction of breast complications during puerperium.

Friday

T. J. Ryan, J. F. Dougherty and J. B. Claffey—9. General surgery, operative and dry clinic.
J. A. Kelly and D. C. Geist—9. General surgery, operative and dry clinic.
D. C. Geist—10. Nerve lesions due to trauma.
A. E. Bothe—11. Tumors of the bladder.

ST. LUKE'S AND CHILDREN'S HOSPITAL

Tuesday

D. Roman, R. W. Larer, H. K. Roessler and staff—9. Thyroid clinic; general surgical operations.
E. A. Tyler—9. Anesthesia, demonstrations.
Warren C. Mercer—9. Gynecological clinic.

Dry clinic—2

E. W. Robertson. The heart and vascular system in relation to abdominal surgery with special reference to gall-bladder surgery.
D. W. Kramer. Diseases in metabolism in relation to surgery.
S. L. Immerman. Recognition of postoperative pulmonary complications.

Wednesday

L. Averett and staff—9. Obstetrical and gynecological operations.
L. F. Milliken—9. Renal lithiasis in which renal sympathectomy has been done or might be done to prevent recurrence of stones.

Thursday

A. W. Hammer, S. Handcock and E. H. Dench—9. General surgical operations.
William C. Hunsicker, Sr. and staff—9. Genito-urinary clinic.
Warren C. Mercer and staff—3. Obstetrical clinic.

Friday

J. A. Brooke and staff—9. Orthopedic operations and demonstration of cases.

CHESTNUT HILL HOSPITAL

Tuesday

Franklin L. Payne—9. Gynecological surgery.
J. F. McCloskey, J. A. Lehman and J. M. Elizey—10. General surgery.
Robert Cadman—3. Allergy in surgical diagnosis.
F. K. Alexander—4. Demonstration of unusual X-ray films.

Wednesday

William B. Swartley, S. Dana Weeder and Stephen Woolston—10. General surgery.
Edward Schuman and Z. B. Newton—10:30. Obstetrical operations.

Thursday

William C. Sheehan, L. H. Hergesheimer and Hans May—10:15. General surgery.
Owen Toland, H. C. Wood and W. Tompkins—11. Obstetrical clinic and demonstration of cases.
Alexander Randall, Frederick Schofield and Frank Massiniso—2. Genito-urinary surgery.
Josephus T. Ullon, Edward McCloskey and Frank M. Ramsey—3. Symposium on surgical failures.

Friday

Francis C. Grant—9. Neurosurgery.
Staff—10:30. Presentation of cases showing interesting bone lesions in traumatic surgery.
Edward F. Corson—1:30. Dermatological clinic, skin lesions in surgery.

WOMAN'S HOSPITAL

Monday

Eleanor Balph—1. Urological clinic.

Tuesday

Margaret Sturgis—9. Sterility clinic.
Margaret Sturgis, Eleanor Balph and Helen Angelucci—10. Gynecological operations.
Dorothy Case Blechschmidt—2. Breast clinic, demonstration of cases, X-ray films, follow-up studies, methods of diagnosis, discussion.

Wednesday

Margaret Sutley—9. General surgical operations.
Alberta Peltz—10. Prenatal obstetrical clinic, toxemias of pregnancy, open discussion.
Lida Stewart Cogill—2. Obstetrical analgesia.

Thursday

Dorothy Case Blechschmidt—9. General surgical operations.

Daily Demonstrations

B. M. Meine. Pathological exhibit.
Mary Easby. Electrocardiological demonstrations, studies of its value in cases of surgical risk.
Dorothy Case Blechschmidt—2. Motion pictures of abdominal surgery.

ABINGTON HOSPITAL

Wednesday

Alexander Randall—9. Urological operations.
D. B. Pfeiffer, C. Smythe, J. W. Levering, I. Boykin, J. M. Deaver, George M. Piersol and Dr. Eiman—2. General surgical clinic. Operations and demonstration of cases.

HAHNEMANN HOSPITAL

Tuesday

L. T. ASHCRAFT, W. C. HUNSICKER and staff—9. Operative clinic: Nephrostomy; prostatectomy; transurethral resection, Caulk-McCarthy punch; demonstration of sacrocaudal block; choice of anesthetics in urological surgery. Presentation of cases of renal pathology, pyelographic studies; vesical neoplasms, results of radiation and endovesical therapy, presentation of cases, urograms and cystograms; a resumé of experimental studies in cortical representation of vesical function, illustrated; demonstration of pathological specimens.

A. B. WEBSTER—9. Fracture clinic.

Wednesday

H. L. NORTHROP—2. General surgery, motion picture demonstration.

Thursday

W. M. SYLVIS—9. General surgery.
THOMAS L. DOYLE—9:30. Plastic surgery.
JOHN BROOKE—2. Orthopedic clinic.

Friday

G. A. VANLENNEP—9. General surgery.
J. M. SCHOFIELD—2. Diseases of the rectum.

Days to be announced

WILLIAM KISTLER. Gastric pathology, demonstration of the Wolf-Schündler flexible gastroscope.

FITZGERALD-MERCY HOSPITAL

Tuesday

J. A. KELLY and T. J. RYAN—9. General surgery.
W. B. HARER—11. Gynecology.

Wednesday

B. R. BELTRAN and A. BURKE—9. General surgery.
J. MISSETT—11. Gynecology.

Thursday

J. A. KELLY and T. J. RYAN—9. General surgery.
J. MCGLINN—11. Gynecology.

Friday

B. R. BELTRAN and A. BURKE—9. General surgery.
W. B. HARER—11. Gynecology.

FRANKFORD HOSPITAL

Tuesday

L. D. ENGLERTH—9. General surgery.
W. E. PARKE—10:30. Gynecological operations.
GEORGE C. HANNA and associates—2. Obstetrical clinic.

Wednesday

W. E. PARKE—9:30. Gynecological clinic.

Friday

L. D. ENGLERTH, B. H. CHANDLEE and R. W. LORRY—9. Fracture demonstration.

SURGERY OF THE EYE, EAR, NOSE, AND THROAT

WILLS EYE HOSPITAL

Monday

FRANK C. PARKER—2. Operations.
THOMAS A. O'BRIEN—2. Dry clinic.

Tuesday

FRANCIS H. ADLER—1. Operations.

Wednesday

THOMAS A. O'BRIEN—2. Dry clinic
FRANK C. PARKER—4. Operations

Thursday

F. H. ADLER—1. Operations.

Friday

THOMAS A. O'BRIEN—2. Operations.
F. C. PARKER—2:30. Operations.

Days to be announced

ALFRED COWAN. Slit-lamp technique.
MILTON J. GRISCOM. Unusual external diseases.
EDMUND B. SPAETH. Plastic surgery of the eyelids.
LEIGHTON F. APPLEMAN. Testing for phorias.

MISERICORDIA HOSPITAL

Monday

J. R. BRENNAN—2. Nasal hyperesthesia, treatment by zinc ionization.

Wednesday

GABRIEL TUCKER—2. Bronchoscopic clinic.

Thursday

C. T. MCCARTHY—2. Three cases of lateral sinus thrombosis with recovery.

Friday

J. A. LOFTUS—2. Mastoidectomy.

FITZGERALD-MERCY HOSPITAL

Monday

C. T. MCCARTHY—2. Otolaryngology.

Tuesday

H. S. BUSLER—2. Otolaryngology.

Wednesday

J. LOFTUS—2. Otolaryngology.

Thursday

C. T. MCCARTHY—2. Otolaryngology.

Friday

H. S. BUSLER—2. Otolaryngology.

WOMAN'S MEDICAL COLLEGE HOSPITAL

Wednesday

CHEVALIER JACKSON and EMILY L. VAN LOON—9. Bronchoscopic clinic.

GRADUATE HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Monday

GEORGE M. COATES—2. Nose and throat surgery.

Tuesday

RALPH BUTLER—2. Nose and throat surgery.

Wednesday

GEORGE B. WOOD—2. Nose and throat surgery.
LUTHER C. PETER—2. Ophthalmological surgery.

Thursday

RALPH BUTLER—2. Nose and throat surgery.

JEFFERSON HOSPITAL

Tuesday

H. H. LOTT—9. Nose and throat operations.
CHARLES E. G. SHANNON—2. Eye operations.

Wednesday

LOUIS H. CLERF—9. Bronchoscopic clinic.
AUSTIN T. SMITH—10. Nose and throat operations.

Thursday

A. J. WAGERS—9. Nose and throat operations.
LOUIS H. CLERF—12:30. Bronchoscopic clinic.

Friday

CHARLES E. G. SHANNON—3. Eye operations.

ST. LUKE'S AND CHILDREN'S HOSPITAL

Monday

J. W. POST and FRANK W. BURGE—2. Clinical and X-ray study of bronchography.

Wednesday

GEORGE MACKENZIE—2. Nose and throat operations.
PHILIP S. STOUT—2. Tonsillectomy by eversion method; modified radical mastoid.

Thursday

S. H. BROWN, F. C. PETERS and staff—2. Ophthalmological operations.

Friday

S. A. BRUMM and staff—2. Nose and throat operations

PRESBYTERIAN HOSPITAL

Monday

G. M. COATES, W. L. CARISS and staff—1:30. Otolaryngology.
H. M. LANGDON, J. THORINGTON and staff—3. Ophthalmological operations and demonstration of cases.

Wednesday

G. M. COATES, W. L. CARISS and staff—1:30. Otolaryngology.

HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Tuesday

GABRIEL TUCKER—9. Bronchoscopic clinic.
Staff—2. Nose and throat operations, demonstration of cases and conference.

Thursday

Staff—2. Nose and throat demonstrations and conference.

Friday

GABRIEL TUCKER—2. Bronchoscopic clinic.

EPISCOPAL HOSPITAL

Monday

J. A. BERTOLET and staff—2. Nose, throat and sinus surgery.
ANDREW KNOX—2. Diseases of the eye.
K. A. KASPER—4. Anatomy of the nasal accessory sinuses.

Tuesday

N. M. BRINKERHOFF—2. Ophthalmological operations.

Thursday

OTTO HIRST and staff—2. Nose, throat and sinus surgery.
N. M. BRINKERHOFF—2. Eye clinic.

WOMAN'S HOSPITAL

Monday

EMILY L. VANLOON—2. Bronchoscopy clinic: Rôle of bronchoscopy in treatment of asthmatic cases, showing of X-ray films and case discussions.
HENRIETTA TANNER—3. Ear, nose and throat operations.

Thursday

MARY BUCHANAN—2. Surgery of the eye, removal of cataract.

HAHNEMANN HOSPITAL

Tuesday

H. S. WEAVER and staff—2. Otolaryngological clinic.

Wednesday

H. S. WEAVER and staff—2. Otolaryngological clinic.

Thursday

H. S. WEAVER and staff—2. Otolaryngological clinic.

CHILDREN'S HOSPITAL OF DREXEL HOME

Days to be announced

RALPH BUTLER. Mastoids in children.
J. A. BABBITT. The problems of the nose and throat in children.

FRANKFORD HOSPITAL

Thursday

FRANK EMBERY and associates—2. Ear, nose and throat clinic.

CHESTNUT HILL HOSPITAL

Tuesday

JOHN B. DAVIES and GEORGE T. FARIS—2. Otolaryngological operations.

Wednesday

B. D. PARISH and F. TRAGANZA—2. Otolaryngological surgery.

Thursday

CARL WILLIAMS—1:30. Ophthalmological surgery.

Friday

CHEVALIER JACKSON—9:30. Bronchoscopy.

ST. AGNES HOSPITAL

Monday

G. F. J. KELLY—4. Eye clinic.

Tuesday

L. D. SULLMAN and A. A. S. GIORDANO—12:30. Nose and throat clinic.

Thursday

L. D. SULLMAN and A. A. S. GIORDANO—12:30. Nose and throat clinic.

Friday

G. F. J. KELLY—12:30. Eye clinic.

JEWISH HOSPITAL

Monday

A. BRAV—1. Ophthalmological clinic.

Thursday

H. M. GODDARD—2. Submucous resection with nasal suction curette.

Friday

A. BRAV—1. Ophthalmological clinic.

COOPER HOSPITAL
(Camden, N. J.)

Monday

J. S. SHIPMAN and staff—2. Eye surgery.

Wednesday

O. R. KLINE, L. B. HIRST and J. P. BRENNAN—2. Nose and throat surgery.

METHODIST EPISCOPAL HOSPITAL

Tuesday

WALTER ROBERTS and staff—2. Otolaryngological operations.

CHILDREN'S HOSPITAL

Days to be announced

A. FEWELL. Ophthalmological surgery.